VOL. 35 NOVEMBER 1959 NO. 11

# BULLETIN

## OF THE NEW YORK ACADEMY OF MEDICINE

*Original Articles by*

BRIAN F. HOFFMAN

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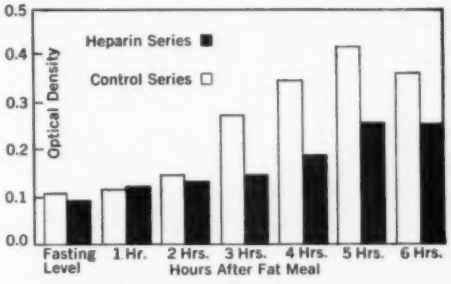


Average serum optical density in 36 patients after fat meal with and without sublingual heparin.[2]


1. Fuller, H. L.: Angiology 9:311 (Oct.) 1958.
2. Shaftel, H. E., and Selman, D.: Angiology *10*:131 (June) 1959.


*Registered trade mark. Patent applied for.

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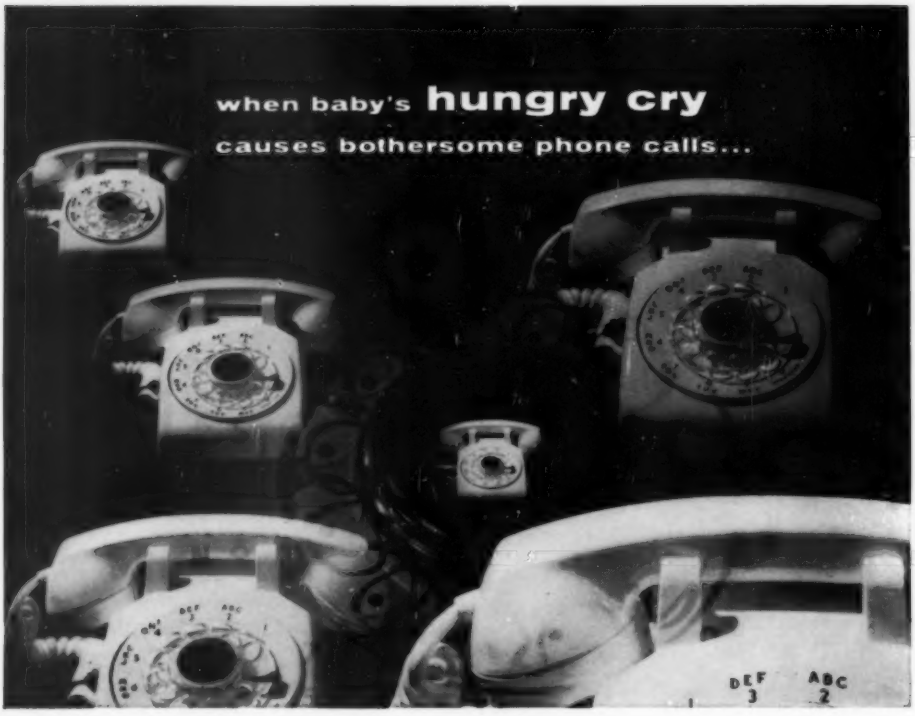


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*Maltose-dextrins formula modifier, Mead Johnson

1. Hatfield, M. A.; Simpson, R. A., and Jackson, R. L.: J. Pediat. 44: 32-45 (Jan.) 1954. 2. Frost, L. W., and Jackson, R. L.: J. Pediat. 39: 580-592 (Nov.) 1951. 3. Henrickson, W. E.: GP 8: 51-56 (Oct.) 1953. 4. Litchfield, H. R.: Arch. Pediat. 61: 617 (Dec.) 1944.

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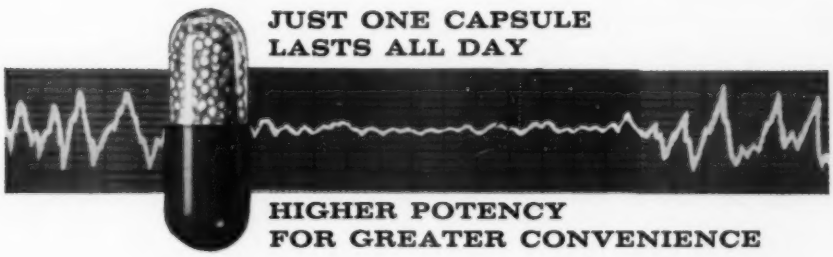


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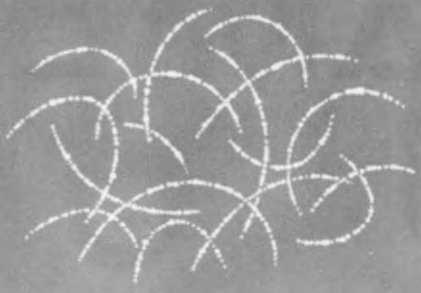

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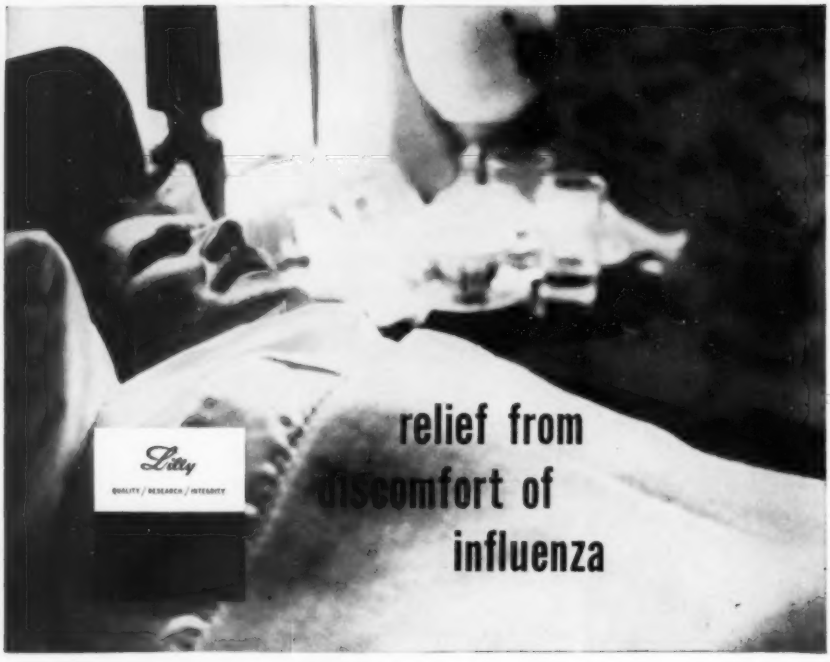


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AUTHORS ALONE ARE RESPONSIBLE FOR OPINIONS EXPRESSED IN THEIR CONTRIBUTIONS

ROBERT L. CRAIG, *Editor*

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BULLETIN OF
THE NEW YORK ACADEMY
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VOL. 35, NO. 11 NOVEMBER 1959

# ELECTROPHYSIOLOGY OF SINGLE CARDIAC CELLS*

BRIAN F. HOFFMAN

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THE subject of cardiac electrophysiology is old, but much if not all of the experimental material on which this lecture is based has been obtained within the past nine years. The technical advance which made possible the study of electrical activity of single cardiac fibers was the development of the microelectrode by Ling and Gerard[1]. A microelectrode is a glass capillary drawn to a tip diameter of less than one micron at one end and filled with a concentrated solution of potassium chloride. The tip of such an electrode can be inserted through the membrane of the cardiac fiber without causing appreciable injury[2]. The electrolyte solution makes electrical contact with the interior of the fiber and the glass capillary acts as an electrical insulator. When such an electrode is paired with another extracellular electrode, it is possible to record the transmembrane potential from single fibers in all parts of the heart.

The potential difference across the membrane of a resting fiber is

* Presented at the Scientific Session of the New York Heart Association, held at The New York Academy of Medicine, November 25, 1958.

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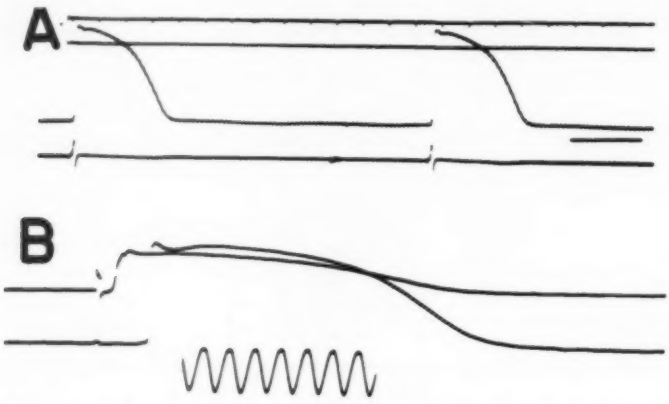


Figure 1—A. Isolated dog papillary muscle. Top trace shows time marks at intervals of 100 and 500 msec. Next trace is line of zero potential. Third trace from top shows transmembrane action potential recorded from a single fiber through an intracellular microelectrode paired with an indifferent electrode. Bottom trace shows electrogram recorded with a unipolar surface electrode adjacent to the microelectrode. B. Isolated cat papillary muscle. Simultaneous records obtained through a small suction electrode (upper trace) and an intracellular microelectrode (lower trace). Equal amplification for both traces. Stimulus artefact precedes the action potential. Sine wave represents 100 mv. and 60 c.p.s.

called the resting potential; that seen during normal activity is called the transmembrane action potential. The type of record obtained when a microelectrode is paired with an external electrode is shown in Figure 1A. When the microelectrode is just outside the membrane of a ventricular fiber, propagated electrical activity is recorded as a typical cardiac electrogram showing R and T deflections. After the electrode has penetrated the membrane, the record shows a steady potential difference, with the inside of the fiber negative to the outside. This potential difference amounts to about 90 mv. in most cardiac fibers. With the onset of electrical activity, the record of the transmembrane potential shows a rapid depolarization, which continues until the inside of the fiber is positive by about 20 to 30 mv. with respect to the outside. This phase of reversed membrane polarity is often referred to as the overshoot. The transmembrane potential then returns to zero and remains steady for 50 to 100 msec. This phase of the ventricular action potential is usually called the plateau, and is followed by a phase of fairly rapid repolarization which restores the normal resting potential. If the local electrogram is recorded at the same time and from the same

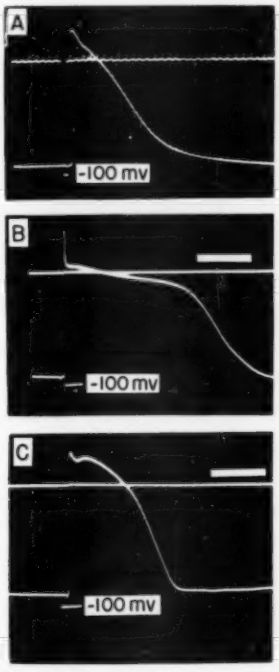


Figure 2—Transmembrane action potentials recorded from single fibers of dog heart. A—Atrium; B—Purkinje fiber; C—Ventricle. Time calibration in A on line of zero potential at intervals of 10 and 50 msec. Horizontal bar in B and C represents an interval of 100 msec.

location as the transmembrane action potential, it is seen that depolarization is simultaneous with the intrinsic deflection of the R complex and repolarization with the T deflection[3]. It is also apparent that the transmembrane action potential is strikingly similar in its voltage-time course to the more familiar monophasic action potential recorded between normal and injured muscle[4]. A comparison of records obtained through an intracellular microelectrode and a small suction electrode[5] is shown in Figure 1B.

The transmembrane action potentials recorded from single fibers of atrium, ventricle and Purkinje system are similar in magnitude but are quite distinctive with respect to shape and duration (Figure 2). In most mammalian hearts, the record of electrical activity obtained from a single atrial muscle fiber does not show a prominent plateau, but in

other respects it differs little from the ventricular transmembrane action potential[6] of the same heart. The transmembrane potentials recorded from single Purkinje fibers, on the other hand, have several distinguishing characteristics[2]. The resting potential is greater than that recorded from fibers of atrium or ventricle, the rate of depolarization is more rapid and the overshoot is larger. Moreover, at slow to moderate heart rates, the Purkinje fiber action potential is considerably longer than that of ventricular muscle; this is due largely to the duration of the plateau, but in part also to the final phase of repolarization. The difference in duration of ventricular and Purkinje fiber action potentials persists even at rapid heart rates or in the presence of ventricular extrasystoles, and thus limits the transmission of activity from ventricular muscle into the specialized conducting system[7].

A variety of studies has shown that, in single fibers of nerve and skeletal muscle, maintenance of the normal resting potential depends primarily on the concentration gradient of potassium across the fiber membrane and the selective permeability of the resting membrane to this ion[8]. If the resting potential of cardiac muscle is similarly created by a potassium concentration gradient across a membrane predominantly permeable to this ion, the approximate magnitude of the potential at 37° should be given by the relationship:

$$E = 61.5 \log_{10} \frac{[K_i]}{[K_o]}$$

where $K_i$ and $K_o$ are the concentrations of potassium inside and outside the fiber. Since the ratio of potassium concentrations in mammals is 30:1,

$$E = 61.5 \log_{10} \frac{30}{1} = 92 \text{ mv.}$$

Thus, the predicted and measured resting potentials are reasonably similar. Moreover, if the extracellular potassium concentration is increased, the resting potential falls as a linear function of the log of the extracellular concentration (Figure 3). When the extracellular potassium concentration is decreased below normal, the resting potential usually falls or remains unchanged (Figure 3). If permeability of the membrane to $K^+$ is increased, however, by addition of acetylcholine[9] or by calcium depletion[10], the resting potential in low potassium solutions comes considerably closer to the predicted value.

The upstroke of the action potential of nerve and vertebrate skeletal muscle has been shown to result from an increase in permeability of the

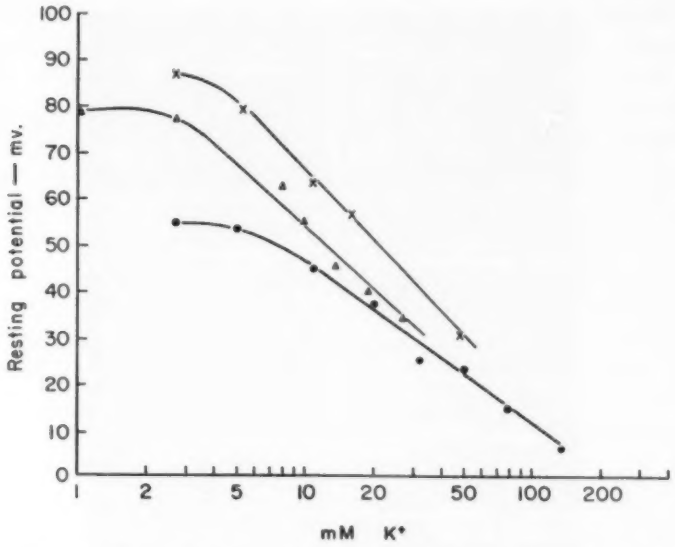


Figure 3—Effect of the concentration of extracellular potassium on the resting transmembrane potential of single fibers. Ordinate = resting potential in mv; abscissa = extracellular K+ concentration in mM/liter. o-o = cat atrium (redrawn from Burgen and Terroux, 1953). x-x = dog papillary muscle. Δ-Δ = rabbit atrium. Each point represents the average of three or more determinations. The extracellular Ca++ concentration in mM/l. for these experiments was as follows: o-o = 1.9; x-x = 2.7; Δ-Δ = 1.9.

membrane to $Na^+$ and a sudden influx of this ion[11]. The evidence for the cause of the action potential upstroke in cardiac muscle is less conclusive[12]. However, in Purkinje fibers Weidmann[13] has demonstrated a marked drop in the electrical resistance of the membrane during depolarization. Also, in Purkinje fibers and ventricular muscle, both the maximum rate of rise of the action potential and amplitude of the reversal are decreased when the extracellular sodium concentration is lowered[2, 14, 15]. Although there is some disagreement between theory and the effect of sodium depletion on tissues from various parts of different hearts[12], nevertheless the effect of a marked lowering of the extracellular sodium concentration on the transmembrane action potential of single cardiac fibers (Figure 4) strongly supports the concept that the change in transmembrane potential on stimulation is due to positive charge carried inward across the membrane by $Na^+$.

The mechanisms responsible for the subsequent voltage-time course

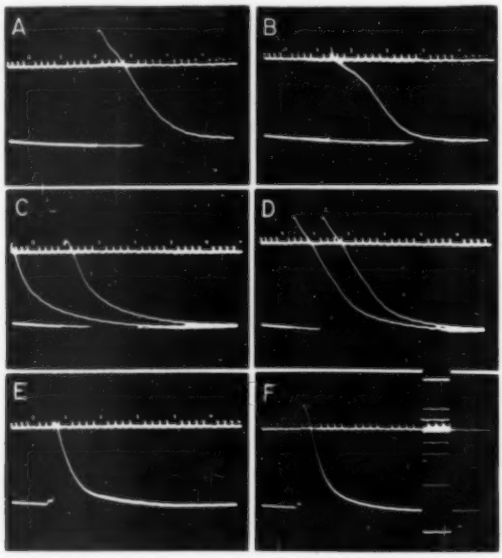


Figure 4—Transmembrane potentials recorded from single fibers of dog atrium showing the effects of decreasing the extracellular sodium concentration. Top trace represents line of zero potential and shows time calibrations in intervals of 10 and 50 msec. Voltage calibration in F = +50, +20, +10, —10, —20, —50 and —100 mv. A—control; B—50% NaCl replaced by sucrose; C—75% NaCl replaced by sucrose; D—return to 100% NaCl; E—75% NaCl replaced by choline chloride; F—return to 100% NaCl. All records obtained 25-30 minutes after changing solutions. See text for discussion.

of the cardiac action potential are less certain. Weidmann[13] has shown that the electrical resistance of the Purkinje fiber membrane increases during the plateau to three times the resting value and then returns to normal during repolarization. Wilde[16] has demonstrated a periodic loss of fiber potassium from the perfused turtle heart more or less synchronous with the S-T segment and T wave. Thus, it is tempting to assume that the current responsible for repolarization of heart muscle is an outward current of $K^+$ similar to that shown for the squid giant axon[17, 18], and that the relatively steady membrane potential during the plateau results from low membrane permeability to both $Na^+$ and $K^+$. However, there is no clear evidence for an increase in permeability of the cardiac fiber membrane to potassium during the phase of rapid repolarization[12, 13]. The postulated potassium efflux may thus result solely from the change in transmembrane potential[13]. Moreover, there are many

aspects of repolarization of cardiac fibers which remain unexplained. Among these perhaps the most suggestive are the marked differences in the voltage-time course of recovery in different types of fibers (see Figure 2), the effect of heart rate and temperature on the duration of the plateau[3, 19] and the shortening of the cardiac action potential caused by a sudden increase in the extracellular potassium concentration[20]. Also of considerable interest is the demonstration that repolarization can be initiated by an anodal stimulus of appropriate strength applied at any time during the plateau of Purkinje fibers[21] or ventricular muscle fibers[22], and that anodal currents weaker than this seem to cause a regenerative change in membrane potential, both during the plateau and during the terminal phase of repolarization[22]. These observations require some revaluation of the apparent decrease in membrane permeability during the latter part of the plateau suggested by impedance measurements.

A number of investigators have related the excitability of a single cardiac fiber to the transmembrane potential, and several aspects of this work are of particular interest. Jenerick and Gerard[23], in studies of single muscle fibers, showed that excitation depends upon the lowering of the resting potential to a certain critical value which they called the threshold potential. This observation contrasts with the idea that an effective stimulus is one which displaces the membrane potential by a fixed amount, regardless of the value of the resting potential. It has been shown with reasonable certainty that excitation of cardiac muscle similarly depends upon lowering the transmembrane potential to a certain critical value which can be called a threshold potential[24]. This demonstration aids considerably in understanding the mechanisms responsible for changes in excitability as well as the spontaneous firing of cardiac pacemakers. If we consider excitability in terms of the current requirement for an electrical stimulus, a change in excitability may result from a change in the value of the threshold potential or the resting potential or both, as well as from a change in the current voltage relationship of the membrane. For example, an increase in the extracellular concentration of calcium has been shown to lower excitability by reducing the value of the threshold potential[24], while calcium depletion enhances excitability by raising the threshold potential and thus bringing it closer to the resting potential. A moderate increase in the extracellular concentration of potassium increases excitability primarily by decreasing the resting potential at a time when the threshold potential is unchanged.

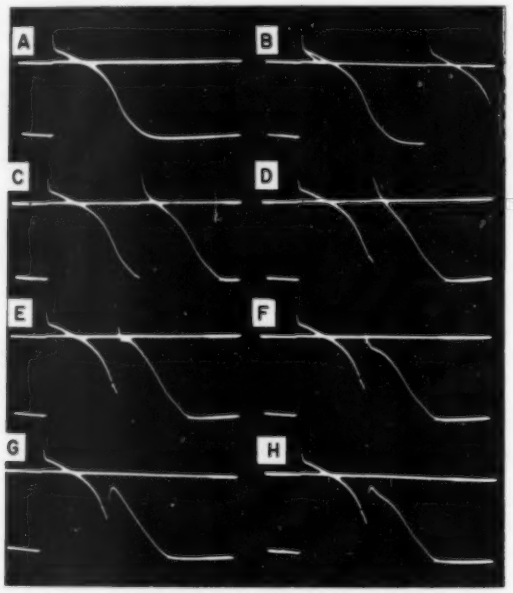


Figure 5—Transmembrane action potentials recorded from a single dog Purkinje fiber showing a normal response (A) and graded responses to stimuli applied at various times during repolarization (B-H).

On the other hand, the changes in excitability which follow excitation depend largely on other mechanisms. In cardiac muscle, as in nerve, the maximum density of the inward sodium current with results from a given depolarization depends primarily on the level of the resting potential prior to stimulation. This relationship depends upon inactivation of the sodium transport system at low levels of membrane potential[11]. Under steady-state conditions, the relationship between the maximum rate of rise of the action potential and the magnitude of the resting potential is described by an S-shaped curve with maximum rates of rise at resting potentials above 90 mv., one-half maximum at -70 mv. and complete "inactivation" at resting potentials lower than 40-50 mv.[14]. For this reason, the recovery of excitability during repolarization depends largely on the level of the transmembrane potential. The absolute refractory period lasts from the upstroke of the action potential until repolarization has restored the membrane potential to approximately -45 to -55 mv. Stimuli applied later during repolarization elicit responses

which are graded both with respect to rising velocity, amplitude and duration (Figure 5). The end of the effective refractory period, when the response to a stimulus becomes propagated, appears at a transmembrane potential of -65 -70 mv.[7], and full recovery of excitability is coincident with the full restoration of the resting potential.

This sort of a description of the recovery of excitability, which employs the level of transmembrane potential rather than the stimulus strength required at various times after the upstroke of the action potential, presents several advantages[7]. For example, it is possible to make direct comparison between excitability in tissues which have action potentials of different shapes and durations and to understand the effects of many agents, such as local anesthetics or antiarrhythmic agents, which have profound effects of excitability but cause little change either in the duration of refractoriness or in the stimulus current required for a response[24].

Use of intracellular microelectrodes to record the transmembrane potentials of single fibers have clarified many other aspects of the excitability of the cardiac muscle. Weidmann[21] has shown that the supernormal period appears before the end of repolarization and that a supernormality results from the restoration of a normal threshold potential at a time when the transmembrane potential is less than the resting value. Recent studies have shown that the refractoriness of cardiac muscle to applied cathodal stimuli and to propagated action potentials is the same (Figure 5)[7], and have given a clearer idea of the safety factor of propagation in cardiac muscle. Several of the interesting effects of anodal stimulation of heart muscle have also been studied using intracellular microelectrodes. The anodal supernormality observed during the dip of strength-interval curve[6, 22] has also been demonstrated by stimulating a single cardiac fiber through one intracellular electrode and recording the transmembrane potential through another (Figure 6). Also, it has been shown that when premature repolarization is initiated locally by application of a pulse of anodal current, this early repolarization propagates throughout the extent of the preparation both in isolated Purkinje fibers[21] and in ventricular muscle [22]. The possibility of propagated repolarization in the intact heart, although not yet demonstrated, is of considerable interest.

In addition to studies such as those just described, the intracellular microelectrode has been indispensable in recording the electrical activity

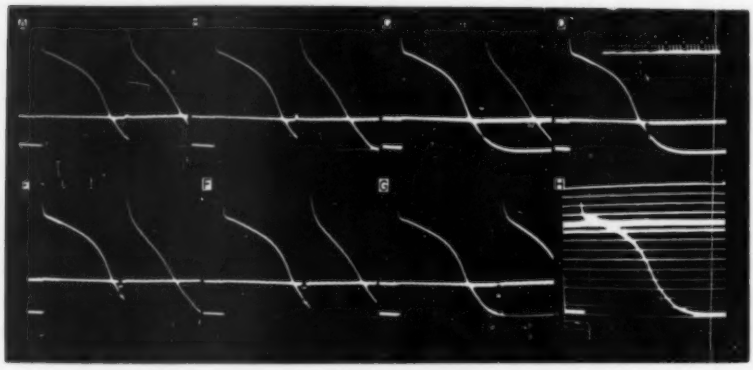

Figure 6—Transmembrane action potentials recorded from a single isolated dog Purkinje fiber through one intracellular microelectrode and effects of stimuli applied through another intracellular microelectrode. Current strength of stimuli is shown by the amplitude of the rectangular pulse on the upper trace. A-C: Response to threshold cathodal stimuli applied progressively earlier during repolarization. D: Ineffective strong cathodal stimulus. E: Weak anodal stimulus (downwards deflection) applied at same interval as cathodal stimulus of D evokes response. F-G: Increasing threshold to anodal stimuli applied progressively later during repolarization. H: Voltage calibration in steps of 10 mv. Time calibration shown in D in intervals of 10 and 100 msec.

of single fibers of the sino-atrial node[25] and the atrioventricular node[26-28], and thereby demonstrating the mechanisms responsible for pacemaker activity in the former tissue and the site and nature of conduction delay in the latter. In Figure 7 the transmembrane potential recorded from a single atrial muscle fiber is compared to the record obtained from a single pacemaker fiber in the sino-atrial node of the rabbit heart. Several marked differences are apparent. Most important, the record from the pacemaker fiber does not show a steady level of resting potential during diastole. Instead, after reaching a maximum value at the end of the phase of repolarization, the transmembrane potential of the pacemaker fiber decreases slowly until, at the level of the threshold potential, the slow depolarization merges smoothly with the upstroke of the locally arising action potential. This type of slow depolarization was first recorded from single pacemaker fibers in isolated bundles of Purkinje tissue[2] and from single fibers in the sinus venosus of the frog heart[29]. The same change in transmembrane potential is seen in records from all cardiac pacemakers, both normal and ectopic, as well as in spontaneously active excitable cells of other types. Slow diastolic depolarization is thus the mechanism underlying the intrinsic rhythmicity of cardiac muscle.

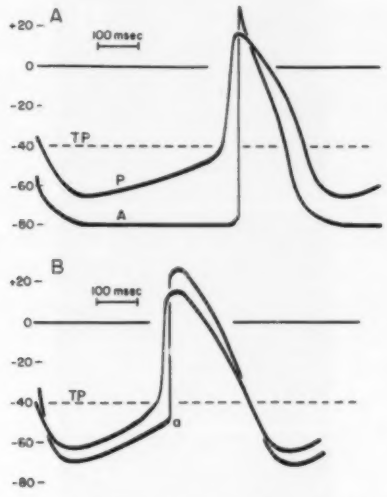


Figure 7—Tracings of transmembrane action potentials recorded from single fibers of rabbit heart. A: Pacemaker fiber of the sino-atrial node (P) and atrial muscle fiber (A). B: True pacemaker fiber and latent pacemaker. Note sharp inflection at (a). Time calibration as indicated. Voltage calibration in millivolts. TP represents level of threshold potential.

In the typical mammalian heart, many fibers show more or less slow depolarization during diastole. Surrounding the sino-atrial node there is a large group of fibers which show marked diastolic depolarization and are best classified as latent pacemakers (Figure 7). They differ from the true nodal pacemakers in that slow depolarization is interrupted, at a level of membrane potential greater than the threshold potential, by the rapid upstroke of the propagated action potential. When pacemaker activity in sino-atrial fibers is arrested, cells in this group assume the role of pacemaker. In addition to these fibers, which have action potentials intermediate in shape and amplitude between sino-atrial node and atrial muscle, there are specialized fibers distributed around the margin of the sino-atrial ring which also show some slow diastolic depolarization and may become true pacemakers under appropriate conditions[30]. Fibers in the bundle of His as well as in the peripheral Purkinje system reveal little or no slow diastolic depolarization under normal conditions. However, either of these fiber types can become a pacemaker. This event is always associated with the appearance of slow diastolic depolarization

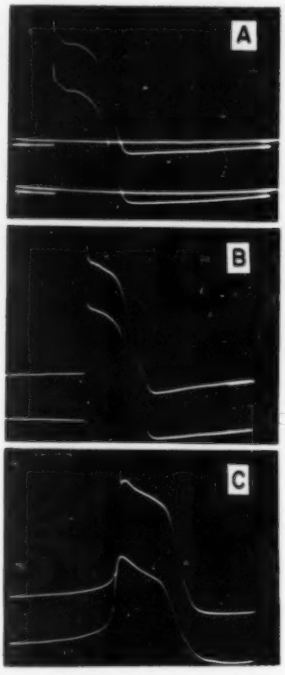


**Figure 8—Transmembrane action potentials recorded from two different locations in a single isolated dog Purkinje fiber. A: Record in Tyrode solution showing slow diastolic depolarization terminating in a steady level of membrane potential. B & C: Effects of l-epinephrine, 1:100,000. Note increase in slope of slow depolarization and appearance of pacemaker-type action potential on lower trace in C.**

and a concomitant decrease in the velocity and amplitude of the action potential upstroke (Figure 8). The appearance of pacemaker activity has not been observed in the ordinary muscle fibers of either atrium or ventricle. The mechanism which causes slow diastolic depolarization and permits spontaneous initiation of impulses thus appears to be restricted to specialized cardiac tissues.

Transmembrane potentials recorded from fibers of the sino-atrial node characteristically reveal a low resting potential, slow rising phase of the action potential and the reduced or absent overshoot. The second and third of these characteristics may be directly caused by the low resting potential, since Weidmann[14] has shown that rising velocity and amplitude of the cardiac action potential are decreased if the resting

potential is lowered. Also, there are many similarities between action potentials of pacemakers and premature action potentials elicited in other cardiac fibers by stimulation during the terminal phase of repolarization (See Figure 5). However, the cause of the low resting potential of these pacemaker fibers is uncertain. From what has been said about the dependence of the resting potential on potassium, it might be assumed that the low value recorded from fibers in the sino-atrial node is caused by a reduced permeability of the membrane to potassium or a low fiber content of this ion. An alternative possibility is that the resting membrane of fibers in the sino-atrial node is more permeable to sodium than is the case in atrium or ventricle, and that the augmented inward $Na^+$ current subtracts from the potential difference caused by a normal potassium concentration gradient and potassium permeability. Unfortunately, there have been no studies of the membrane resistance of single sino-atrial fibers; also, accurate information on the content of $Na^+$ and $K^+$ of nodal fibers is not available. It has been observed, however, that the resting potential of nodal fibers is changed only slightly by an increase in the extracellular potassium concentration from 2.7 to 13 mM., and that pacemaker activity persists, although under this condition adjacent atrial muscle is depolarized and inexcitable[31].

Also unexplained is the mechanism responsible for slow diastolic depolarization. Weidmann[32] has demonstrated a progressive increase in membrane resistance of Purkinje fibers during the phase of slow depolarization, suggesting a decrease in ionic permeability. An increasing sodium permeability as a cause of depolarization is thus unlikely, even though a lowered extracellular concentration of $Na^+$ abolishes slow depolarization in Purkinje fiber pacemakers[2]. This result would be expected regardless of the membrane characteristics directly causing slow depolarization, and merely shows that there is some inward $Na^+$ current during the period of slow depolarization. Moreover, in Purkinje fibers, potassium excess decreases and potassium depletion augments slow diastolic depolarization, while in the sino-atrial node a comparable change in the concentration of either $Na^+$ or $K^+$ has little if any effect on pacemaker activity. In summary, although most of the evidence suggests that pacemaker activity is directly related to altered ionic permeability and most likely a decreasing permeability to potassium, a clear experimental demonstration of this mechanism is lacking.

Records of the transmembrane potentials of pacemakers suggest at

least three distinct mechanisms which will influence heart rate. The cycle length will be increased if the slope of diastolic depolarization is reduced, if the threshold potential is decreased or if the resting potential is increased. Obviously, changes in the cycle length may also result from a simultaneous change in more than one of these factors. Each of these mechanisms has been shown to operate under certain conditions. The effects of autonomic mediators are primarily on the slope of slow depolarization; vagal stimulation decreases and sympathetic stimulation increases the rate at which the membrane potential approaches the threshold level[33-35]. Acetylcholine acts in much the same manner as vagal stimulation, although a difference between amphibian and mammalian hearts has been noted. In the former[34, 35], vagal stimulation causes an actual hyperpolarization of the pacemaker membrane. In the rabbit atrium, on the other hand, arrest of a sino-atrial pacemaker by acetylcholine is associated with a steady level of membrane potential between the maximum resting potential and the threshold level. Concurrently, the pacemaker site shifts to some other area in either the atrium or upper His bundle. This effect of acetylcholine on pacemaker tissue is apparently due to an increase in the permeability of the membrane to potassium [35, 36]. The resulting augmented $K^+$ efflux would be expected to maintain a higher resting potential regardless of the ionic currents responsible for slow depolarization, and, as in the case of sodium depletion, supplies only suggestive evidence for the cause of pacemaker activity. The increase in rate caused by sympathomimetic agents resembles that resulting from sympathetic nerve stimulation. In both instances, acceleration is due primarily to an increase in the rate of diastolic depolarization, although the level of the threshold potential has been reported to increase, remain constant or decrease[37-39]. This latter observation is difficult to evaluate because of concomitant shifts in the pacemaker site. Both epinephrine and nor-epinephrine are equally potent in accelerating a sino-atrial pacemaker or in producing pacemaker activity in previously quiescent Purkinje fibers (Figure 8), and in high concentrations both agents cause multifocal pacemaker activity in the specialized conducting system[6].

The slope of diastolic depolarization of Purkinje fibers is influenced markedly by changes in temperature, while the threshold potential remains the same[19]. Moderate changes in the extracellular concentration of calcium alter the frequency of Purkinje fiber pacemakers mainly by

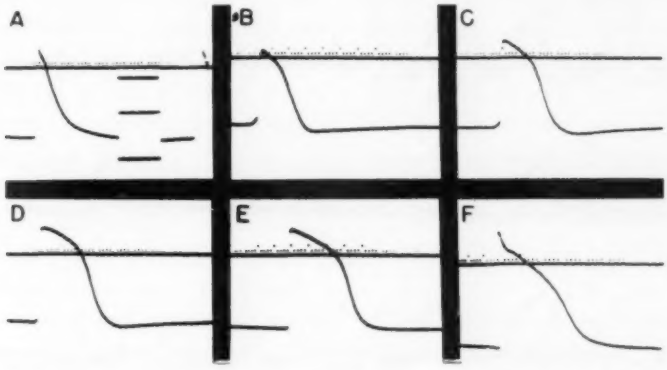


Figure 9—Transmembrane action potentials recorded from single fibers of atrium (a), upper node (b), mid and lower node (c, d, e) and upper His bundle (f). Upper trace represents line of zero potential and shows time calibration in intervals of 10 and 50 msec. Voltage calibration in (a) from above down, shows in mv: —10, —50 and —100. Overshoot in (a) is larger than that commonly recorded. See text for discussion.

raising or lowering the threshold potential; with extreme calcium depletion, however, the slope of diastolic depolarization is increased and multifocal pacemaker activity ensues. Sino-atrial pacemaker fibers are relatively insensitive to cooling, and regular activity persists after propagation in atrial muscle has failed because of a reduced resting potential[40]. Under these conditions, addition of acetylcholine increases the resting potential in atrial muscle and restores propagation of the activity originating in the sino-atrial node. This mechanism would seem to explain the observations reported a number of years ago by Bülbring and Burn[41]. Records obtained from single Purkinje fibers by means of an intracellular microelectrode have helped explain the antiarrhythmic action of quinidine and procaine. Both these agents, in concentrations which do not cause any important change in the amplitude of the resting potential or the amplitude, rising velocity or duration of the action potential, decrease the slope of diastolic depolarization in Purkinje fiber pacemakers. This effect is the same whether pacemaker activity has appeared spontaneously or in response to sympathomimetic agents. In higher concentrations, toxic effects of these same agents, such as conduction delays and appearance of extrasystoles, can be shown to result from a decrease in the rising velocity of the action potential and an actual enhancement of slow diastolic depolarization.

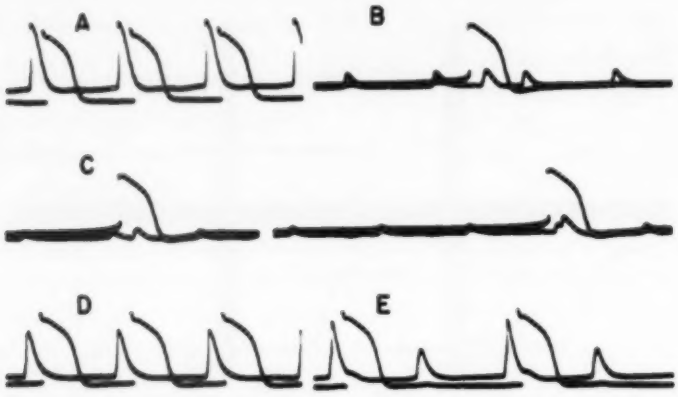


Figure 10—Transmembrane action potentials recorded from a single fiber of the atrioventricular node (top trace) and bundle of His (bottom trace) of the rabbit heart. A: Control. B-E: Segments of a continuous record showing the changes produced by acetylcholine added at B. Note decrease in amplitude of nodal response (B), complete a-v dissociation and appearance of pacemaker activity in the bundle of His (C) and 2:1 relationship between activity in nodal and His bundle fibers (E) during washout of the acetylcholine.

One problem in cardiac electrophysiology which has been studied by a variety of techniques is the nature of normal atrioventricular delay. Use of intracellular microelectrodes to record from single fibers of atrium, atrioventricular node and bundle of His has recently provided new information on the site and cause of this delay. Transmembrane potentials recorded from single fibers at the atrial margin of the A-V node have been found to show several distinctive characteristics. In addition to a low resting potential and some slow diastolic depolarization, these fibers show a slowly rising action potential with a slurred, notched upstroke and small or absent reversal (Figure 9)[26, 27]. Between this site and the upper His bundle, the action potential shows a gradual transition in amplitude and shape; and in the bundle of His the action potential is similar in configuration to that recorded from peripheral Purkinje fibers (Figure 9).

The major part of the normal atrioventricular delay is due to the slow spread of activity through fibers at the atrial margin of the node[27, 28]. Partial and complete block due to acetylocholine, high rate or hypoxia results from partial or complete failure of transmission at this site (Figure 10)[27, 28]. Records obtained from single nodal fibers during normal and altered A-V transmission suggest that, at the atrial

margin of the node, conduction is decremental because of the anatomical arrangement and physiological properties of the fibers at that location[27, 28]. On the other hand, block of retrograde transmission from ventricle to atrium has been shown to take place, at least under some conditions, at the peripheral junction between ventricular muscle and the Purkinje fibers[7, 42]. During complete atrioventricular dissociation, however, if pacemaker activity originates in fibers of the bundle of His, failure of transmission to the atrium is localized to the atrial margin of the node. All of these findings are in remarkably good agreement with the early postulates of Erlanger[43].

In conclusion, use of intracellular microelectrodes to study single cardiac muscle fibers has provided answers to many classical problems in cardiac electrophysiology. Also, as is the case with each technical improvement, the ability to record the transmembrane potential of single cardiac fibers has also given rise to new challenges and new questions which can only be answered by further technical advances.

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# HISTORICAL BACKGROUND OF THE NEUROLOGICAL INSTITUTE AND THE NEUROLOGICAL SOCIETIES*

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Professor Emeritus, Clinical Neurological Surgery,
College of Physicians and Surgeons, Columbia University, New York, N.Y.

A fiftieth anniversary seems perhaps more than any other to have a twofold significance—a goal attained and a starting point for new achievement. I am honored to have the opportunity of speaking on such an occasion in the annals of the New York Neurological Institute. Your President has suggested as my subject the relationship of the New York Neurological Society and the Section on Neurology and Psychiatry of The New York Academy of Medicine to the Neurological Institute. This assignment gives me a particular satisfaction, for to speak of the relation of these societies to the Institute is to speak of the men who created them. It thus affords me an opportunity to pay homage on behalf of the Neurological Institute to the distinguished neurologists who laid the foundations upon which it has built so effectively and, incidentally, to express my own indebtedness to the men who placed New York in the vanguard of our specialty in America. Carlyle has said: "In every man's writings the character of the writer must lie recorded." So the character of the founders is reflected in the institutions that grew from their efforts.

To review the work even of the more illustrious of our members would carry me far beyond the time at our disposal. For the sake of the record, I should like at least to mention the names of Edward Spitzka, Landon Gray, George Beard, John Shaw—referred to by Spitzka as "Cardinal to the Pope Seguin"—Bernard Sachs, Israel Strauss, Smith Ely Jelliffe, Ramsay Hunt, George Jacoby, Edward Fisher, Foster Kennedy, Walter Timme, and Edwin Zabriskie. I shall refer at greater length to William Hammond, Edward Seguin, Allen Starr, and

* Presented, March 10, 1959, at a combined meeting of the Section on Neurology and Psychiatry and the New York Neurological Society, at The New York Academy of Medicine, in commemoration of the Fiftieth Anniversary of the Neurological Institute of New York of the Columbia-Presbyterian Medical Center.

Frederick Tilney, who from 1870 to 1938 held successively the chair of neurology in the College of Physicians and Surgeons, and to Charles Dana, Professor of Nervous Diseases at Cornell. These men played a dominant role in American, and specifically New York neurology, not alone by virtue of their teaching activities, but also through their numerous contributions to the fund of neurological knowledge.

Organized neurology in New York dates from 1872. There was at that time a galaxy of eminent neurologists in this city, ten of whom formed the New York Neurological Society. It was not until 1874, however, that the Society became an actual working organization. On March 10 of that year, exactly 85 years ago to the day, Dr. William Hammond issued the following call to the neurologists of New York:

Dear Sir:

It is contemplated to reorganize the New York Neurological Society (instituted March 1872), and you are respectfully invited to cooperate in this work.

Probably no department of medicine is advancing with greater rapidity than that which relates to the Physiology, Pathology and Therapeutics of the Nervous System. It is not doubted that there are, in this city and its vicinity, many who will take such an interest in this society as to render it of great service to medical science.

Believing you to be of this number, this circular is addressed to you, in the hope that you will become one of the original members.

Should you accede to this proposal, please address a note to that effect, at your earliest convenience, to either of the undersigned.

Due notice will be given of the first meeting of the society.

Respectfully

Your obedient servant.

William A. Hammond, 43 W. 54th Street
Alexander Murray, 23 East 10th Street
J. Marion Sims, 267 Madison Avenue
J. C. Peters, 83 Madison Avenue
Max Hertzog, 48 West 34th Street

Forty-three physicians responded and met with signers of the invitation on April 6, 1874, in the rooms of the Medical Library and Journal Association, 107 East 28th Street. Dr. J. C. Peters was asked to occupy the chair temporarily and Dr. George Wells was appointed Secretary *pro tem.* At the request of Dr. Peters, Dr. Hammond set forth the purpose of the meeting, namely to revive the New York Neurological

Society—which beyond the transaction of some business of minor importance had accomplished nothing in the two years of its existence—and to "proceed to active work". Dr. Hammond was elected President of the revivified society, with Dr. John C. Peters as First Vice-President; Dr. J. Marion Sims, Second Vice-President; Dr. George D. Wells, Recording Secretary; Dr. Max Hertzog, Corresponding Secretary; Dr. Alexander Murray, Treasurer; Drs. J. H. H. Burgh, D. B. St. John Roosa, J. M. B. Cross, F. D. Lente, and S. LeRoy Satterlee, Councilors.

The second meeting was held May 4th, 1874, with an inaugural address by the President entitled "The Effects of Alcohol on the Nervous System", a subject which the Society is still investigating on occasion, in one way or another. The motto, *Fabricando Fabri Fimus* (We achieve in doing), suggested by Hammond, was now to become its guiding principle.

This was the first Neurological Society in America. The Philadelphia Neurological Society was founded in 1884, with Weir Mitchell as its somewhat reluctant President, and the Neurological Society of London in 1886, with Hughlings Jackson as President.

Less than a year after the founding of the New York Neurological Society another call was issued by William Hammond and six of his colleagues, four of them from New York, which led to the formation of the American Neurological Association. As contemplated by its founders, this was to be a national association for the cultivation of the neurological sciences, the number of members not to exceed 50. Thirty-five men signified their acceptance, 16 of whom were New York neurologists.

The first eleven meetings of the American Neurological Association were held in New York City; the second, third and fourth meetings at the College of Physicians and Surgeons, then at Twenty-third Street and Fourth Avenue; the remainder at The New York Academy of Medicine, then at 12 West 31st Street.

Dr. Hammond, a genial host, at the first meeting and on a number of subsequent occasions invited the members to dine at his home. These early gatherings were the forerunners of the annual dinner which in former years contributed so much to the close relationship among the members of the Society.

I trust I shall be forgiven if I digress here to refer to one or two of these occasions which have become a part of the Society's tradition. It

VANDERBILT CLINIC, 1888

is related that while Landon Carter Gray, a reserved, dignified, even austere figure, was President, his attention at dinner was diverted while those beside him filled his pockets with silver from the table. Suddenly he was seized by a "Constable" and William Osler began pulling silver out of his pockets, saying: "Item one, 2 silver spoons; item two, 2 silver forks; item three, knife—all marked A C, property of the club—and finally a pepper and salt shaker."

At another meeting, William Keen, an ardent prohibitionist, was present. Suddenly, when the evening was well along, one of the members seized him and stood him on one end of the table, another crowned him with a wreath of leaves after Bacchus, and others came forward to pour libations at his feet.

History apparently *does* repeat itself, for on still another evening some years ago, Dr. Henry A. Riley and I decided that our beloved Adolph Meyer, then seated at the speaker's table, adorned with a lei and a hula-hula skirt, would speak more eloquently if he were lifted upon the table. With some trepidation we proceeded to put our idea into effect. It may be said that Adolph Meyer never made a more telling speech than on that occasion, and no one seemed to enjoy the episode more than he.

To return to more serious matters, on April 13th, 1885, eleven years after the reorganization of the New York Neurological Society, the Section on Neurology of The New York Academy of Medicine was formed. Abraham Jacoby, then President of the Academy, held that its individual sections should play a more important role and, since no section of neurology existed, urged that one be instituted. Of the 12 sections now existing, the one on neurology and psychiatry is the third oldest. The first meeting took place April 13, 1885.

> "In response to a call of the President of the Academy of Medicine, the following members of the Academy met at No. 12 West 31st Street at 8:30 P.M., April 13, Drs. Amidon, Bull, Corning, Gibney, Jacoby, Leo, E. A. Maxwell, J. C. Peters, Putzel, Seguin and Graeme Hammond.
>
> "Dr. Peters was temporarily installed as Chairman. He inquired as to the object of the meeting. Dr. Gibney then stated that as a part of the endeavor to centralize medical work about the Academy, it had seemed desirable to him that a neurological section be started. This step was taken not in a spirit of controversy with any existing organization for he thought that there were both men and material enough in New York to make interesting two neurological meetings a month. The Academy had as members many who were deeply interested in neurology who had pledged themselves to give the section their support. In conclusion he moved that a section of neurology be organized.
>
> "After some discussion as to the title of the section the motion was carried.
>
> "The officers were then elected as follows: Chairman, Leopold Putzel; Secretary, Graeme Hammond.
>
> "It was then decided that the meetings should be held on the second Friday evening of each month, excepting July, August and September. Upon motion it was voted that for the present the members of the section bear the expenses of printing cards giving notice of meetings, etc.
>
> "On motion the section then adjourned."

During the intervening years the New York Neurological Society and the Section on Neurology of the Academy of Medicine have worked together in a happy union to advance the science of neurology and its cognate subjects.*

* The records of a meeting of the Council of the Neurological Society, February 4, 1878, bring to light an amusing conflict with the Academy. At that meeting a discussion took place as to the charge by the Academy for the use of its small parlor. The Academy apparently charged the New York Neurological Society five dollars for each of the summer months from June first to November first, when no meetings were held. To this the members objected. As if this were not enough, on one occasion when the small parlor was not ready, they were compelled to use the large hall and were charged an extra fee. After considerable discussion it was stated that "if such sharp practices are to be followed by the Academy of Medicine, it is our opinion that the sooner we break our contract the better . . at the rate charged at present, we will soon be obliged to close the society altogether". The Academy relented and agreed that the New York Neurological Society could occupy the small parlor for five dollars an evening and not be charged for the summer months, when no meetings were held.

The two New York societies from their beginning manifested an interest in public affairs affecting their specialty. In July 1874, Dr. Hammond gave the results of the postmortem findings in a case of hydrophobia, remarking fully upon the histology and exhibiting microscopic sections. A series of resolutions was passed by the New York Neurological Society and a committee was appointed to make an investigation as to the cause, prevention, and treatment of this condition. In December 1874, in further pursuit of this matter, the Society unanimously adopted a proposal to prevent the passage of legislation offered by the Society for the Prevention of Cruelty to Animals, praying that no such legislation should receive the countenance of the Legislature of the State of New York.

In February 1878, following presentation of a paper by Edward Spitzka criticizing the management of the insane in the State of New York, with particular reference to the evils of restraint, the Society appointed a Committee on the Insane, consisting of Hammond, Gray, Spitzka, Morton, and Harwood, to present to the State Senate a petition containing the complaints deemed most important, and requesting a thorough investigation of *all* institutions for the care of the insane in the State, so that "the broad light of day should shine upon the whole subject".

At its annual meeting on January 1, 1901, the New York Neurological Society again concerned itself with the management of the insane. The society recommended the creation of one central laboratory where the best scientific men in the various departments of medicine could devote themselves exclusively to original research in pathology, neurophysiology, psychology, chemistry and anthropology. It was felt that their studies and publications, from year to year, would advance the treatment of the insane and be a credit to the State as a patron of science which foreshadowed Dr. Adolph Meyer's appointment as Director of the Pathological (Psychiatric) Institute on Ward's Island.

William Hammond, the prime mover in the organization of the New York Neurological Society, may certainly be designated the outstanding figure in the early history of neurology not only in New York but also in America. He was born in 1827, son of a physician and descendant of two old Maryland families. He began the study of medicine at sixteen, was graduated (1848) from New York University at twenty with the degree of M.D. and then served an internship in the Pennsyl-

vania Hospital. He was in the Army from 1849 to 1860 and during this period, in spite of many difficult assignments, was able to devote some time to physiological research. His paper on the "Nutritive Value and Physiological Effects of Albumen, Starch and Gum When Singly and Exclusively Used as a Food" won for Hammond the American Medical Association prize in 1857.

His many attainments attracted the attention of the University of Maryland and in 1860 he resigned from the Army to accept the Chair of Anatomy and Physiology in that institution. With the outbreak of the Civil War, he resigned his professorship and rejoined the Army, not with the high rank he had earlier attained, but as an assistant surgeon at the foot of the list. His great ability and the backing of the important Sanitary Commission, however, won him prompt promotion to the office of Surgeon General. In this position he made many notable and far-seeing changes in the medical department of the Army. In May 1863 he created a separate Army hospital for the treatment of nervous diseases and nerve injuries, the first such institution to be established in an American army, the command of which he asked his colleague and friend Silas Weir Mitchell to share with George Morehouse. In recognition of this achievement and the far-sighted vision which prompted it, Weir Mitchell in 1872 dedicated his book "*Injuries of the Nerves and Their Consequences*", to Hammond. The Board of Medical Examiners was reorganized and the standards for applicants for the medical department were raised. Hammond also directed the organization of an Army Medical Museum, recommended the establishment of a permanent general Army Hospital in Washington, and instituted a military medical library. While carrying on the burdens of the Surgeon General's office, he began the *Medical and Surgical History of the War of the Rebellion*, as well as publishing a volume of more than 500 pages on military medicine and surgery.

Hammond's many innovations and dynamic personality plus the fact that his appointment had been urged upon Secretary Stanton over the heads of others, including the latter's own choice, inevitably led to conflict with the autocratic Secretary of War. Stanton issued orders relieving Hammond of his Washington post, though retaining his rank as Surgeon General, and assigned him to New Orleans. Hammond demanded restoration of his office or court martial. It is said the court martial found for acquittal but a reconsideration was directed and

Hammond was then dismissed. In 1878, at a rehearing, his conduct in office was vindicated and his rank as Brigadier General was restored by an act of Congress. His portrait in full dress uniform now hangs in the National Library of Medicine.*

On Hammond's return to New York after the termination of his Army career, his knowledge and skill as a neurologist won for him a lectureship at the College of Physicians and Surgeons, and subsequently a professorship was created for him at Bellevue Hospital Medical College. Not only was he recognized as a stimulating teacher, having an easy flow of language and a commanding personality, but his great ability earned for him a dominant role as a neurologist and, as we have seen, as a builder and organizer of neurology, not only in New York but in America. He was the first to describe athetosis, in 1871, and in 1890 his son, Graeme Hammond, presented the pathological findings of the case on which his father had based his original description. One hundred twenty-five other papers and sixteen books were written by Hammond, covering a wide variety of subjects: "On Pigmentary Deposits in the Brain Resulting from Malarial Poisoning"; "Myxoedema with Special Reference to Cerebral and Nervous Symptoms", which contained the first reference to the endocrine system; "Spinal Irritation, Posterial Spinal Anaemia"; "Thalamic Epilepsy"; "Mysophobia"; "Seven Recent Cases of Brain Surgery"; "The Effects of Alcohol upon the Nervous System"; and "Fasting Girls, their Physiology and Pathology". These and many other contributions earned him a national reputation.

Hammond's *Diseases of the Nervous System*, published in 1871, was the first American treatise on neurology and went through nine editions, being translated into French, Italian, and Spanish. *Spiritualism and Allied Causes and Conditions of Nervous Derangements* appeared in 1876. The object of this book, as stated by its author, was "to strip from the basis of fact, which at most always exists, the network of error which ignorance, credulity, and superstition have woven around it. . . . There can be no conflict between pure science and pure religion, for the one is truth, and the other is faith in truth." Previously Hammond had published *Physiological Memoirs* in 1863, and *Military Medical and Surgical Essays* for the U. S. Sanitary Commission in 1864. Finally, his

* This record is almost the exact counterpart of the trials and tribulations of John Morgan, Director General of the American Medical Department during the Revolution, when the intrigue and antagonism of William Shippen culminated in Morgan's unjust dismissal in 1777. Two years later Morgan was honorably acquitted by a court of inquiry. He was a graduate of Edinburgh, a member of the French Academy of Surgery and a Fellow of the Royal Society.

*Treatise on Insanity in its Medical Relations* appeared in 1893. From 1867 to 1869 he edited the *Quarterly Journal of Psychological Medicine* and, from 1870 to 1876, its successor, the *Journal of Psychological Medicine*, which in 1873 became the *Psychological and Medico-Legal Journal*.

Hammond was outspoken in expressing his opinion, with little fear of the consequences. He had something of a flair for showmanship. One of his public experiences brought forth the following editorial in the *Psychological and Medico-Legal Society Journal*, then edited by Allen McLane Hamilton:

> "Quite recently, several public-spirited medical members of the medical profession, with a very considerable desire to expose spiritualism, invited a young man to demonstrate to a mixed audience how the tricks were performed. An introductory address by Dr. Hammond, whose name had been advertised throughout the city for a week previously, and an organ solo introducing the Star Spangled Banner, by a well-known organist, drew a great many curious people together. Dr. A. B. Mott and two other medical men tied up the medium in a skillful manner, and the affair was witnessed by a large number of the profession. We would take the liberty of suggesting that it would be much more dignified, and proper, if such investigations hereafter were made by committees from the Medical Societies, and, if necessary their reports could be subsequently given to the public."

While Hammond was the driving force in the creation and organization of neurology as a specialty, he had as a contemporary and coworker Edward Seguin, whom Mills of Philadelphia considered to be "the best clinician I have ever known". When Mills was summarizing his views on cerebral localization in 1888, he referred to Seguin's numerous contributions as ranking "first in American medical literature", and Dana told young medical men that, if they wanted to succeed, they should study the lives of Seguin, father and son.

Edward Constant Seguin was born in 1843, son of a distinguished father, Edouard Seguin, who came to this country from Paris in 1850. The younger Seguin was cradled in neurology, having studied medicine under his father before entering the Medical School of Columbia University from which he was graduated in 1864. He served on hospital ships as a dresser before the age of nineteen and subsequently as a medical cadet during the Civil War.

After Seguin's service in the Army and a medical residency, he studied abroad under Brown-Séquard, Charcot, Ranvier and Cornil.

WILLIAM ALEXANDER HAMMOND
*Courtesy of The National Library of Medicine*

EDWARD CONSTANT SEGUIN
*Courtesy of The New York Academy of Medicine*

Under Ranvier he developed an interest in neuroanatomy and histology, and under Cornil became interested in the pathology of the nervous system. Imbued with the keen, penetrating clinical principles taught him by Brown-Séquard and Charcot, he returned to New York and became associated with William Draper, Professor of Medicine in the College of Physicians and Surgeons. While with Draper, he devised the first clinical chart in America, calling it a Chart of Vital Signs. It showed in graphic form respirations, pulse and temperature, and was essentially identical with the charts now in use.

After a short period of general practice, Seguin determined to devote himself exclusively to diseases of the nervous system, believing that only by specialization could well qualified observers, with leisure to work in a given field, advance original research. His studies were sadly interrupted by a great personal tragedy. His wife, in a sudden fit of insanity, killed herself and her three children. Seguin retired temporarily to Europe, and during his sojourn there his lectures and clinical papers covering the period from 1866 to 1882 were brought together in a single volume, as *Opera Minora*, by his brother-in-law Robert

Amidon. They were affectionately inscribed by Seguin "To William Draper, Professor of Medicine at the College of Physicians and Surgeons, my friend and master in the clinical art".

Seguin's lectures were models of clarity and logical sequence, frequently closing with a brief historical sketch of the subject under discussion. His instructions on "Methods of the Neurological Examination" could be read today to great advantage.

Seguin's introductory lecture on *Diseases of the Nervous System* (1874) is divided into three sections: 1) The elementary parts of the nervous system—their anatomical attributes and physiological properties; 2) study of the organs and apparatus of the central nervous system and their functions; 3) a summary of the chief modifications of their properties and functions, which constitute the symptomatology of disease. He recognized four general functions of the nervous system: sensation, motion, reflex, and coordination. Questions to be determined by the neurologist were: Is there disease, where is the disease, what is the disease, and lastly, though foremost in importance, what can be done to cure or relieve the patient?

Seguin divided the spinal cord into two physiological and anatomical regions: 1) the anterior half, the kinesodic system, made up of the anterolateral columns and ventral horns, and 2) the dorsal half, the aesthoesodic system, consisting of the posterior column and posterior horns. On this basis he discussed the localization of disease, considering first the two systems, and second the columns or horns within these systems. The advances made in New York in the diagnosis and surgical treatment of diseases of the spinal cord thus owe their origin to Seguin's clear, orderly, and concise teachings. He applied the same principles and methods with equal lucidity to the brain.

In addition to his teaching, Seguin made extensive contributions to the literature covering the entire field of diseases of the nervous system. His paper, "A Contribution to the Pathological Anatomy of Disseminated Cerebrospinal Sclerosis", in 1878, contained detailed histologic studies of the pons, medulla, and spinal cord, showing the early, the more advanced, and finally the most extensive expression of the disease. This was the first American autopsy report of disseminated sclerosis with detailed histologic studies. Among other publications which won for him a reputation as one of the foremost neurologists in the country were papers on "The Relationship of Headache to Choked Disc in

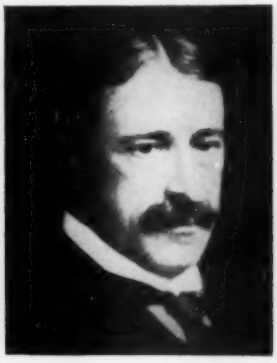
Tumor of the Brain"; "Infantile Paralysis"; "Hysterical Symptoms in Organic Nervous Disease"; "The Efficacy of Certain Drugs in the Treatment of Nervous Disease".

Seguin was also associated with the early days of the Vanderbilt Clinic. This institution, established in 1888 by the four sons of William H. Vanderbilt, with an amphitheatre large enough to accommodate four hundred, and material excelled only by the Salpetrière in Paris and the Charité in Berlin, became the primary source of neurological training in New York. The clinics started there by Edward Seguin after his return to America were later carried forward with great éclat by Allen Starr and Frederick Tilney. During each year, 50 or more forms of nervous and mental diseases were demonstrated and often four to ten patients with any particular disease. The Chiefs of Clinic carried on sectional teaching using the rich material of the clinics. Jelliffe and Brill said of the Vanderbilt Clinic, "After a somewhat extensive experience gained by visits and by exhaustive stays in a number of European clinics including those of London, Paris, Berlin, Munich, Zurich, Vienna, Rome, Naples and Brussels, we believe that, with few exceptions, the work of the clinic compares favourably with that done in the European clinics."

It was there that Joseph Collins, Pearce Bailey and Frederick Peterson, founders of the Neurological Institute, received much of their early training and inspiration in the art of neurology. They felt, however, the great need for a hospital where patients with neurological diseases could be more thoroughly studied and treated.

After long consideration of the possibility of such a hospital, it was determined to obtain the assistance of prominent business men in realizing this aim. Accordingly, on March 9, 1909, Dr. Collins issued an invitation to Mr. Isaac Townsend, Mr. Richard Williams, Mr. Adrian Iselin, Jr., Mr. Otto Kahn, Mr. H. H. Knapp, Mr. Paul Warburg, Dr. Lightner Whitman, and Mr. Robert P. Perkins to meet with him and Dr. Joseph Fraenkel at the Century Club on the evening of March 18 to study the question of providing a hospital in New York City for the care and treatment of nervous and mental diseases. They became the first Board of Trustees and agreed unanimously as to the need for such a hospital, with the result that an application for its establishment was filed with the State Board of Charities and, on April 14, 1909, a certificate of incorporation was granted.

JOSEPH COLLINS



PEARCE BAILEY

FREDERICK PETERSON

Dr. Collins and Dr. Fraenkel were joined by Dr. Pearce Bailey and on May 10, 1910, they drafted a lengthy letter to the Trustees pointing out not only the need of a special hospital devoted to diseases of the nervous system but also the fact that, in addition to those who received treatment, the country at large would benefit from such an institution. It was felt, indeed, that the undertaking would have failed in its chief object if it did not disseminate knowledge of the principles of neurology and act as a center of instruction for physicians who would come to it from all over the country. Copies of this letter were sent to the friends of the Trustees with a personal note, and to the New York newspapers.

Meanwhile a search for a building was under way, and on May 27, 1909, at a meeting in Mr. Richard Williams' office, approval was voted for leasing and putting in suitable condition the structure at 149-151 East 67th Street.

While neither Dr. Charles Elsberg nor Dr. Alfred Taylor was among the founders, they were active in their support of the hospital throughout their lives. Dr. Elsberg was invited to join the staff on December 13th, 1909, after the hospital had been opened, and Dr. Taylor shortly thereafter.

Dr. Collins spent the summer abroad, visiting various neurological clinics and studying their methods, with a view to incorporating the most recent advances in the work of the Neurological Institute. On November 29, 1909, an announcement of the opening of the Institute

NEUROLOGICAL INSTITUTE, 1909-1929

NEUROLOGICAL INSTITUTE, 1929-

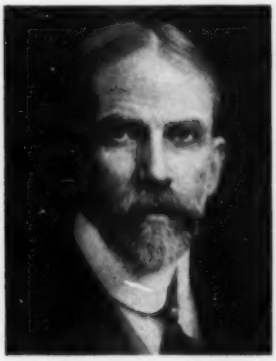
was issued, describing it, in part, as follows:

> "The Hospital consists of two wards, one for males and one for females, into which suitable cases will be received free of charge; of private wards in which the charge for care and treatment will be from ten to fifteen dollars a week; and of private rooms.
>
> "Except in emergency patients will be admitted to the wards of the hospital only after examination by one of the attending physicians. The hours for admission are from two to four daily, except Sundays and holidays.
>
> "The Dispensary will be open daily except Sundays and holidays, from two to four for charity cases only. During these hours one of the Medical Board and his assistants will be in attendance.
>
> "Physicians are invited to send patients suffering from nervous, mental and allied diseases to the dispensary for diagnosis and for treatment, or for admission to the wards. Patients bringing letters from their physicians requesting diagnosis or suggestions in regard to treatment will be referred to their physicians."

Thus the Neurological Institute began its pioneer work—the first hospital with laboratories and operating room facilities on the American continent devoted to diseases of the nervous system, where bedside instruction could be given. In this achievement Joseph Collins' vision,

ALFRED TAYLOR

CHARLES ELSBERG



CHARLES LOOMIS DANA

*Courtesy of The New York Academy of Medicine*

energy, and drive played a dominant role. His efforts in the early organization of the Institute and his continued devotion over the years led many of his colleagues to refer to it as "Dr. Collins' Hospital".

Joseph Collins attended the University of Michigan. While attempting to live on eighteen dollars a month, eight of which went for a room, he acquired pneumonia, followed by an unrecognized empyema which sapped his strength, preventing him from continuing his undergraduate studies. Despite having been forced to abandon his college work, he later entered New York University, from which he received his M.D. degree in 1888, and then studied abroad. On his return he worked in a number of dispensaries, becoming Professor of Neurology at the New York Post Graduate Medical School in 1897, which post he held until 1909, when he resigned to devote his full efforts to the newly founded Neurological Institute. He was a facile speaker and writer, publishing more than 100 papers as well as medical texts and books of a more literary character. In 1897 his *Genesis and Dissolution of the Faculty of Speech*, an elaborate and thorough study of aphasia, won for him the Alvarenga Prize of the College of Physicians of Philadelphia. This book was followed by *Diseases of the Brain*, 1899; *The Treatment of Nervous Diseases*, 1909; *Pathology of Nervous Diseases*, 1901; *The Sympathetic Nervous System*, 1905; *The Way with Nerves*, 1911; and *Sleep and the Sleepless*, 1912.

Collins saw the patient as an individual. "What constitutes disease,"

EDWIN ZABRISKIE

FOSTER KENNEDY

WALTER TIMME

he wrote, "is not a lesion or an infection so much as a man who is in pain, fearful, and apprehensive. The latter, in most instances, should be treated, *not* the disease. . . . Apprehension halts nature, fear fetters her. The physician should not only thwart fear, he should engender courage. . . . The emotions are the motor power of life, the intellect the motor. . . . Two patients with the same symptoms are no more alike than two men who wear the same clothes. . . . Medical schools must eventually teach their students to cope with patients *and* disease, with the psychological problem *and* the pathological specimen." Collins' criticism of physicians was born of his own experiences when sick. Out of these experiences were forged many of his principles of practice. The physician, he felt, too often saw the pathological specimen which he presented, not the psychological problem. "I had attempted to work beyond my strength. I was the victim of the ardents and it required an ardent (Osler) to detect it."

Upon our entry into World War I in 1917, Pearce Bailey asked Collins for his assistance in putting into effect the Elimination Tests at officers' training camps. Collins gladly accepted the assignment, though reluctant to leave their "infant enterprise in 67th Street. Though it had cast off its swaddling clothes and was prancing about dressed conspicuously and becomingly, it still needed discipline and direction".

After a short time at officers' training camps, Collins assumed charge of the medical department of the American Red Cross in Italy. His

experiences in this post are covered in *My Italian Years*, published in 1919, followed in 1920 by *Idling in Italy*. While on one of his journeys through Italy he came upon a monument to Andrea Cesalpino (1519-1603), Professor of Medicine at the University of Pisa, whose discovery of the circulation of the blood is considered by the Italians to antedate Harvey's. Browsing through libraries, Collins finally obtained a copy of Cesalpino's work and wrote an interesting comment, entitled "A Neglected Worthy—Andrea Cesalpino." While Cesalpino apparently knew the circulation in theory, he performed no experiment to establish the fact, nor did he fully grasp its significance. His view had no effect upon medicine.

Dana speaks of Collins as one "whose qualities and character I hold high; among other reasons, because he does things not only for himself but for others; whose social gifts and genial wit outweigh the occasional bursts of a not completely repressed acerbity. I like a man who is not altogether perfect, for this justifies my own self esteem."

When Collins died in 1950, at the age of eighty-four, he left the major part of his estate, over a million dollars, as an endowment to help needy medical students. "I venture to hope that this foundation will give a helping hand to some young man or woman who finds himself in the predicament in which I found myself when I was obliged to turn to teaching in district schools to provide funds to continue my education in medicine."

Pearce Bailey, another of the founders of the Neurological Institute, was graduated from Princeton in 1886 and from the College of Physicians and Surgeons, Columbia University, in 1888, served an internship at St. Luke's, and followed this by study in Vienna and Paris. Bailey became Chief of Clinic at the Vanderbilt Clinic under Allen Starr and Adjunct Professor of Neurology at Columbia in 1906. Upon the founding of the Neurological Institute, he devoted his time mainly to that institution though serving as consultant at St. Luke's and a number of other hospitals.

Bailey's influence at the Neurological Institute has been described as that of a catalyst. Under his stimulation, the Laboratory School and the Classification Clinic were begun. His broad vision, practical common sense, and generous spirit were in constant evidence. He headed the New York State Commission for Mental Defectives, receiving special commendation from Governor Miller for his outstanding services.

Bailey's articles on crime and mental defectives received nation-wide notice, especially one which appeared in the *New York Tribune* entitled "Shall the State Kill Children?", referring to the electrocution by the state of two men with a mental age of six years. His book on *Diseases of the Nervous System Resulting from Accident and Injury*, first published in 1896, revised and enlarged in 1906 and again in 1909, remains an authoritative treatise.

Bailey's work in charge of the Division of Neuropsychiatry in the Surgeon General's office in World War I earned for him and for the service which he established the greatest admiration. The Elimination Tests which he had instituted to weed out the unstable and unfit proved to be most valuable and served as a pattern for similar tests adopted by our allies. These had been preceded by an interesting study, "Efficiency and Inefficiency—a Problem in Medicine". The success of the Division of Neuropsychiatry was largely due to Bailey's ability to judge men, to his organizing genius, and his foresight. For his achievement he was awarded the Distinguished Service Medal on March 12, 1921: "For exceptionally meritorious and distinguished service as Chief of the Division of Neuropsychiatry, Surgeon General's Office, in which capacity he displayed exceptional zeal, foresight, and good judgment in organizing, developing and directing neuropsychiatric work in the Army on a high plane of efficiency."

In the development of the Neurological Institute, Bailey gave unstintingly of his time and energy. His rounds with his staff were seldom missed by any of the members. He was an exponent not only of the art of neurology but of the art of teaching as well. A great part of his time at the bedside was spent in obtaining a complete history; in his view the neurological examination was secondary, the history all important. The comments of his contemporaries are enlightening. Timme said: "Nothing was more characteristic of him, after some long defense of a far-fetched fanciful diagnosis by some member of his staff at rounds, than his smiling indulgent query 'Do you really believe it yourself?'" Peterson said: "His intellect, his wit and his humor have lent a charm to our gatherings. He was respected and admired for his integrity, fearless independence of thinking and for his great courage with which he bore many sorrows."

Bailey's psychological study of Voltaire is of special interest. "Voltaire," he wrote, "possessed better than anyone, the capacity to look

things in the face, and in spite of what he saw there, to maintain with humility the high level of his constructive mental energy. It would be hard to find a more exacting test of intellect and courage than that—to contemplate correctly the verities, and still show undismayed the feelings and actions of an optimist." Those who knew Bailey would recognize in these words a startlingly accurate description of the working of his own mind. These tenets could with equal justice be applied to him.

Joseph Fraenkel, also active in the founding of the Neurological Institute, was born in Russia and came to this country from Vienna, where he received his medical education. He landed in America friendless and nearly penniless, and accepted a post in pathology at the Montefiore Home. In one of the dispensaries he worked with Collins, who found him to have excellent clinical insight and judgment. By virtue of his intellectual honesty, kindliness, and industry he won, in a short time, a commanding practice among wealthy members of the community.

Fraenkel's interests, however, eventually turned to endocrinology; his publications were few, and his influence upon neurology in New York, and particularly upon the Neurological Institute, was negligible if not detrimental. Though one of the original founders of the Institute, he resigned in less than a year, taking with him several of the wealthiest and most generous of the trustees. He had proposed that none of the physicians connected with the Institute be allowed to engage in private practice and that fees be collected by the hospital, which in turn would pay the physicians a salary. This was unacceptable. As a result of his resignation and the withdrawal of several of the wealthy trustees who had been his patients, the institute faced a serious crisis, which fortunately was met by the immediate backing and support of Dr. Charles Dana and Dr. Frederick Peterson.

When Frederick Peterson and Charles Dana stepped into the breach caused by the resignation of Dr. Fraenkel and several of the Board of Trustees in December 1911, they brought to the hospital a stabilizing influence and an unswerving devotion. Dr. Peterson took over direction of the Second Division, from which Fraenkel had resigned, and Dr. Dana became a member of the Board of Trustees.

Frederick Peterson, born in Minnesota in 1859, early decided to become a physician and in 1879 acquired his M.D. degree from the University of Buffalo. After three years of graduate study in Vienna, Zurich, and Strassburg, he returned to America to accept the chair of

pathology at the University of Buffalo. His real interest, however, lay in psychiatry, and in 1885 he joined the State Hospital Service as assistant physician at the Hudson River State Hospital, Poughkeepsie, where he remained for three years. In order to have actual contact with the insane, he believed it important to live with them, and during this period he never left the hospital. Useful occupations were introduced, interests stimulated, and opportunities provided for the patients. Peterson was instrumental in having the name Hospital substituted for Asylum, thus impressing upon the public that mental disorder is a sickness like any other disease. He was the first to advocate a psychopathic hospital for New York City, and in 1901 secured from the city a grant of land at Beekman Place for this purpose.

When, in 1888, Peterson came to New York, he served as Chief of Clinic under Allen Starr at the Vanderbilt Clinic, becoming Clinical Professor of Psychiatry at Columbia in 1903. From 1901 to 1904 he served as President of the New York State Lunacy Commission, in which his administrative ability brought order out of chaos. His appointment of Adolph Meyer as Director of the Psychiatric Institute of the New York State Hospitals in 1903 furthered the scientific progress of the entire State Hospital system.

With Josiah Letchworth in 1890, Peterson founded Craig Colony for Epileptics and, as President of the Board of Managers, was largely responsible for its development, maintaining an interest in its affairs throughout his life.

In 1907 he worked with Jung for two months, though he held many reservations concerning some of the psychoanalytic methods. Sachs said of him: "He refused to be taken off his feet by some of the fantastic doctrines of the day."

Peterson urged "medical students and practitioners not to be so overwhelmed with mechanics and half truths that they lose the power of close clinical observation. . . . I met a patient who had had most of these tests tried on him and he said the experience was most impressive. I asked what the doctor had done for him as a result of these labors. He said: 'He gave me rhubarb and soda, and when I told him that is just what my doctor had given me long ago, he said it was not rationalized, not scientific. Then I replied: Rationalized rhubarb is having a wonderful cathartic effect on my pocketbook.' "

The Child Health Organization was especially dear to Peterson, who

conceived it and maintained an active role in it. "We need but ten minutes of health instruction in our schools—these reach the young child, become a part of him, and affect his whole attitude toward life. . . . The health span of life must be increased, not the span of life with ill health and decrepitude."

Many neuropsychiatric contributions were made by Peterson in addition to his *Textbook of Nervous and Mental Diseases*, which went through nine editions. With Haines he wrote a *Textbook of Legal Medicine and Toxicology* which held a high position in its field.

Peterson was deeply interested in Chinese literature and art, with which he surrounded himself. His *Chinese Lyrics*, printed with reproductions of Chinese art in 1916 under the pseudonym of Pai-ta-shun, was highly praised as the work of a Chinese poet unusually gifted in English. The University of Pennsylvania conferred an honorary Doctor of Laws upon Dr. Peterson on February 22, 1919. The citation read: "Eminent psychiatrist and author of profound works upon the most mysterious mental diseases—lecturer in medical jurisprudence and in toxicology—poet of distinction to whom the literary world is also indebted for hidden gems from the Swedish and Chinese literatures."

Sachs informs us that in May 1938, in Pasadena, Kirsten Flagstad sang Peterson's beloved song "The Sweetest Flower That Grows", before a large audience including the composer, James H. Rogers, and the poet. As the last notes of her wondrous voice died away, Peterson turned to his wife and murmured: "Now lettest thou thy servant depart in peace."

These are the men who built a strong foundation for neurology, and through their vision and foresight created the Neurological Societies in New York and established the Neurological Institute. Their labor has given us a heritage rich in tradition and high in purpose and to us they have bequeathed the challenge of carrying their ideals to even greater fulfillment. To them we are grateful.

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The author regrets that neither time nor space permits him to record the many invaluable contributions to New York neurology and to the Neurological Institute of Drs. Starr, Dana, Elsberg, Zabriskie, Kennedy, and Timme. It is hoped that their influential role may be the subject of a future report.

The author wishes to express his appreciation of the invaluable help given by the entire staff of the Library of The New York Academy of Medicine in the search for source material and to Mrs. Weaver and Miss Thrall for their assistance in arranging the historical exhibit shown in the entrance foyer of the Academy.

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# THE EVOLUTION OF NEUROLOGY*

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Progress in neurology lagged behind other branches of medicine because of the slowness of the development of knowledge regarding the form and function of the nervous system. The brain and spinal cord, covered with a hard, bony shell, are particularly inaccessible to direct examination. The type and nature of disease of these structures could only be inferred from a study of the disorders of function which occurred when they were damaged, until more accurate methods of visualization of details of their intimate structures were discovered. When the techniques of auscultation and percussion were introduced into medicine, these methods were applied to the study of the nervous system. They were rapidly discarded as useless. It is interesting to quote from an article written by James Hope in 1840: "The diseases of the brain are, at the present moment, more obscure than any great class in the nosology. Twenty years ago, the same was said, and with truth, of the diseases of the lungs and heart; but the elucidation and corroboration of the general symptoms by the physical signs derived from auscultation, percussion, etc., have reversed the proposition and not only redeemed these diseases from their obscurity, but actually rendered their diagnosis more precise and certain than that of any other important class. There are no physical signs applicable to the brain; and, from the circumstances in which the organ is placed, it is to be feared that none will ever be discovered."

This pessimism can be understood when one realizes that at this time, the tendon reflexes, plantar responses, and the now well-known signs of dysfunction of the cerebellum, or basal ganglia, had not yet been described.

An adequate examination of the nervous system was not possible

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until the form of the central nervous system had been accurately described and the function of various parts elucidated by surgical ablations, electrical stimulation, and the pathologic study of experiments of nature.

Some knowledge of the function of the brain and spinal cord was known to the ancient physician, but the concept of humors and vital spirits prevailed in the writings of Hippocrates and Galen. Convulsive seizures and headache were the two neurological symptoms which received most attention in the writings of ancient physicians. With the Renaissance, neurology began to advance through the foundation of a scientific anatomy in the 16th century by Leonardo da Vinci and Vesalius. Further advances were made in the 17th century by Willis, Vieussens, van Leeuwenhock, Pacchioni, and others. These men paved the way for the studies in the 18th century which culminated in such fine atlases of the nervous system as that of Soemmerring.

The development of the concepts of the physiology of the central nervous system paralleled to a great extent the growth of knowledge of anatomy. Signal advances were not made, however, until the 19th century. The studies of men such as: Sir Charles Bell, Johannes Muller, E. H. Weber, A. V. Waller, Du Bois-Reymond, Gustav Fritsch, Eduard Hitzig, J. C. Dalton, David Ferrier, John Hughlings Jackson, and others, culminated in the modern neurophysiology typified by the writings of Sir Charles S. Sherrington.

On the background of these advances in anatomy and physiology, neurology began to emerge as a clinical specialty in the middle and latter parts of the 19th century. Guillaume B. A. Duchenne is generally credited with being the founder of modern clinical neurology. He was followed, in France, by J. M. Charcot, Pierre Marie, Josef F. F. Babinski and J. J. Dejerine; in Germany, by M. H. Romberg, W. H. Erb, C. F. O. Westphal, and H. Oppenheim; in England, by John Hughlings Jackson, D. Ferrier, William R. Gowers, H. C. Bastian, Henry Head, and S. A. Kinnier Wilson.

American neurology was cradled in the army and had its start in the period of the Civil War. W. A. Hammond, Surgeon General, during 1862-63, created a special military hospital for nervous diseases, in Philadelphia in 1862. He is credited with writing the first treatise on nervous disease in the English language, in 1871. An independent chair in neurology was established at the University of Pennsylvania in 1876,

with H. C. Wood as Professor of Diseases of the Nervous System. In Boston, James J. Putnam was made Lecturer on Neurology in 1872, but neurology was not separated from medicine at Harvard until 1895. In New York, Edouard Seguin was appointed Professor of Diseases of the Nervous System at the College of Physicians and Surgeons in 1871. Other early leaders of neurology in this country include: C. K. Mills, S. Weir Mitchell and W. G. Spiller, in Philadelphia; and Moses Allan Starr, Charles L. Dana, E. C. Spitka, and Bernard Sachs, in New York.

Although the pathology of the central nervous system was studied in the 17th and 18th centuries, neuropathology did not come of age until the first part of the present century. The names of a few who have contributed to the development of neuropathology include: Alois Alzheimer, Max Bielschowsky, Constantin von Economo, Alfons Jacob, Franz Nissl, Walter Spielmeyer, and Carl Weigert, of Germany; Raymon Y. Cajal and Pio del Rio Hortega, of Spain; Ettore Marchiafava and Giovanni Mingazzini, of Italy; Jean Cruveilhier, of France; Georges Marinesco, of Rumania; J. Godwin Greenfield, of England; and J. H. Globus and W. B. Hassin, of the United States.

On the firm background of anatomy, physiology and pathology, neurology has advanced in the United States from its modest beginnings in three medical schools. At the present time there are independent departments, or specialized sub-departments of neurology, in more than one-half of the schools of this country. The American Neurological Association has grown from a membership of 35 in 1875 to 400 in 1958; and the recently founded American Academy of Neurology has a membership of more than 2,000. In addition, there are special societies for neuropathology, neurophysiology, electroencephalography, and neurochemistry.

Modern clinical neurology is tending to veer away from the minutiae of the neurological examination in favor of a broader study of the patient. The precise localization of the lesion has given way to an analysis of the disturbance of function in terms of the underlying physiological, biochemical and metabolic disturbance. Accuracy of localization by a careful neurological examination is not to be decried, but lesions in the nervous system, particularly in the case of tumor where localization is so important, can now be sharply delimited by electroencephalography, pneumoencephalography, angiography, and myelography. The surgeons, who operate on patients, desire information with

regard to exact extent, blood supply and the like, which can be obtained from these special tests. They are rarely willing to operate on patients without this valuable additional information. The clinicians who deal with other organic and functional diseases of the nervous system now turn to the physiologist and biochemist for aid in the solution of their problems.

Anatomy, physiology and pathology have laid the groundwork. Biochemistry is the field which now offers great promise for the future. This does not imply that the older basic science disciplines should not be nurtured. All have a great deal to contribute to the advancement of our knowledge of the nervous system and it is quite possible that any one of them may ultimately contribute equally as much, or more, to the solution of clinical problems than the more recently developed sciences of biochemistry and biophysics.

# A LOOK AHEAD AT TECHNICAL AND TRAINING DEVELOPMENTS IN NEUROSURGERY*

J. LAWRENCE POOL

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NEARLY 200 years ago John Hunter[1] wrote that he did not greatly mind preparing a paper because "like a tradesman, it is a way of taking stock". In like manner, this discussion takes stock by considering contemporary interests and activities of neurological surgery as a basis for forecasting future trends and training needs.

The foundation of this forecast rests, in part, on a survey of recent neurosurgical literature and in part on a sampling of present work-loads in various neurosurgical clinics and practices. In addition, such a forecast will obviously be influenced by the extent to which modern clinical and technical developments will be applied to neurosurgery. Finally, ideas for improving neurosurgical training, collected from a number of thoughtful colleagues, will be summarized and consolidated in the conclusion of this report.

The Journal of Neurosurgery[2], founded 15 years ago, is an ideal yardstick for assessing trends of neurosurgical interest as illustrated in simplified graphic form in Figure 1, which indicates the number of publications on major topics each year from 1944 to 1959.

A marked interest in clinical and experimental studies of brain, spine and nerve injuries in the years immediately following World War II is shown, followed by a healthy degree of continued attention to trauma. Thus new data on the physiology of cerebral concussion[3] and studies on the prevention of head and neck trauma in automobile accidents[4] have recently been reported. Since there is such an obvious need for further improvement in this field, especially with respect to the treatment of head injuries by drug therapy[5], hypothermia[6] and

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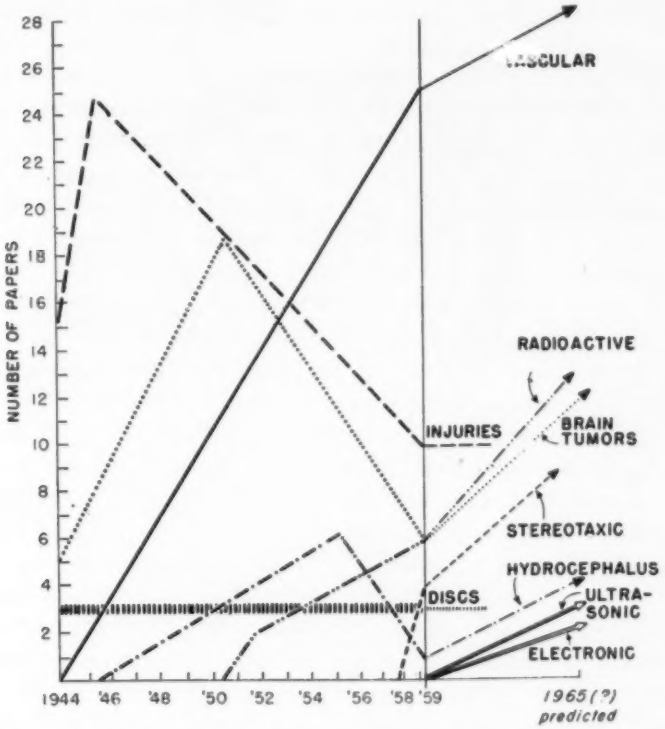


Fig. 1—Interest in various neurosurgical conditions estimated from annual number of papers on each topic in JNS 1944-1958 inclusive.

other means, it is expected that research along these lines will be continued. Promising research on spinal cord and peripheral nerve regeneration is also expected to continue[7].

While brain tumor therapy has received a steady share of attention through the years, interest in this direction recently appears to have waned. With the advent of painless, harmless diagnostic tests, such as improved radioactive scanning techniques and enzyme studies of the cerebrospinal fluid[8], we can now look forward to better results in the management of brain tumors, especially those of the glioma series, because of earlier diagnosis and localization. There is also reason to hope that specific drug therapy will soon be added to radical surgery and

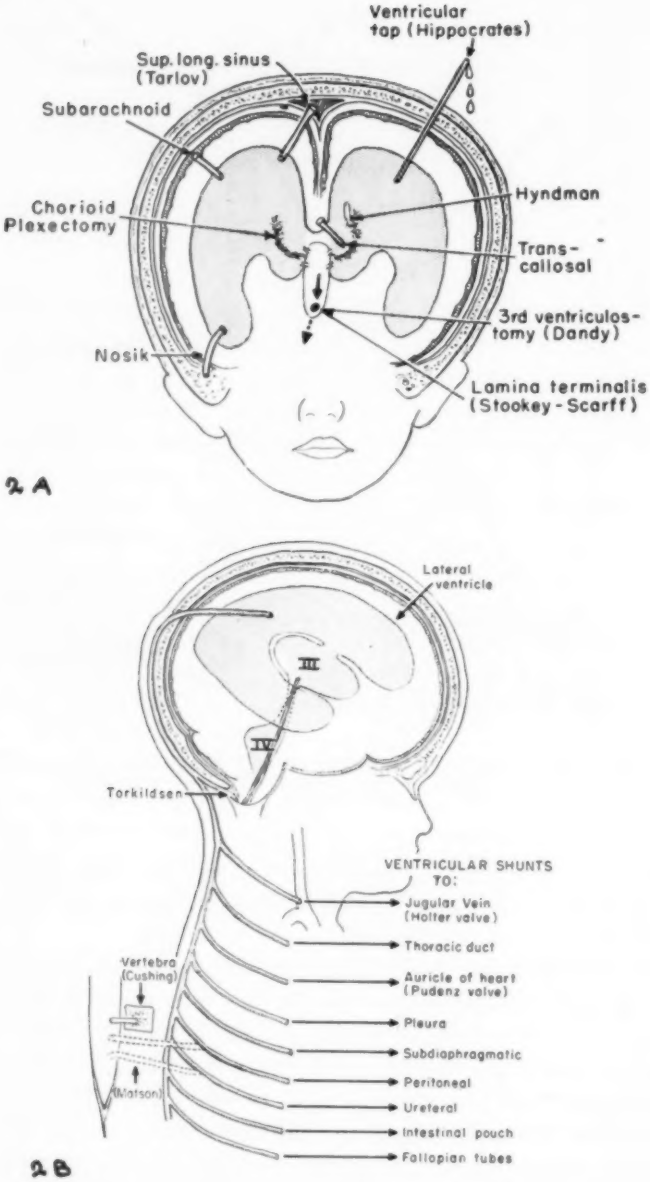


Fig. 2—a & b: Diagrams of procedures tried or currently used for treatment of obstructive and nonobstructive hydrocephalus of various types, including intubation of obstructed aqueduct of Sylvius.

x-ray therapy[9] in the treatment of glioblastoma multiforme and other gliomas and thus further increase our interest in the treatment of brain tumors.

The treatment of various types of hydrocephalus, always of paramount interest to neurosurgeons, should also continue to receive attention in view of the many unsolved problems concerning its production and relief. The very multiplicity of past and current therapeutic measures illustrated in Figure 2 (a, b) points up the need for further investigative and therapeutic efforts. In this respect it is interesting to note that many years ago Cushing[10] went so far as to suggest the need for specialists in the study and treatment of hydrocephalus.

Intervertebral disc surgery, although comprising a goodly amount of neurosurgical work, as we shall see, has received proportionately less attention than traumatic, tumor, or other types of neurological surgery, probably because the pathology and treatment of disc disease is so much better understood. There is room, however, for further work on intervertebral disc problems, such as more efficient methods of diagnosis and conservative therapy, whether or not to do a spinal fusion, whether or not to open a compromised nerve root sheath, or to use the anterior approach.

The most intriguing and challenging problem in neurosurgery at the moment, however, is vascular surgery. As indicated in Figure 1, interest in the dynamics, diagnosis, and pathology of cerebral circulatory disturbances is likely not only to continue but to increase. Well it may, when one considers both its technical fascinations and the many ramifications it offers with respect to the functioning of the cerebral circulation, such as the phenomena of vasospasm[11], reflex cardiac complications[12], brain edema[13], intermittent carotid or vertebral claudication and the like.

Additional trends in neurosurgery include the use of radioactive techniques for studies of the cerebrospinal fluid and blood-brain barrier, for the diagnosis and treatment of brain tumors, and for the creation of focal therapeutic lesions in the brain. We have also become increasingly aware that the diagnostic, experimental and therapeutic applications of focussed ultrasound are only just beginning and that the use of permanently or temporarily implanted electrical devices for diagnostic or therapeutic purposes in various parts of the nervous system has not yet been exploited to an extent commensurate with technical developments

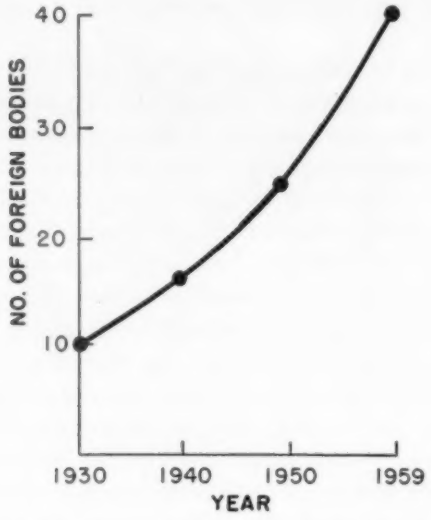


Fig. 3—Foreign bodies used in neurosurgery.

in the science of electricity. Indeed, experimental and therapeutic techniques used to date[14, 15] suggest the possibility that compact electronic apparatus for implantation within the body may be devised to activate structures deprived by injury or disease of their normal neural control.

Technical developments along these and other lines rest entirely on the ability and imagination of future neurosurgeons. Their predecessors have already demonstrated a remarkable degree of ingenuity in this regard, as shown in Figure 3 and Table 1, which illustrate the rather startling array of foreign bodies purposely used in our branch of surgery to save and protect human lives.

As in other branches of medicine the understanding and application of biochemistry is attaining an ever increasing importance in neurosurgery, in the treatment, for example, of glial tumors, severe head injuries, cerebral edema, cerebral vasospasm, pituitary disorders and the spasms of the paraplegic.

An increasing trend in this direction has therefore been indicated in Figure 1. Finally, it may be suggested that the last chapter on the surgery of certain types of epilepsy has not yet been written, and that

TABLE I—FOREIGN BODIES USED IN NEUROSURGERY

| | 1930 | 1940 | 1950 | 1959 |
|---|---|---|---|---|
| Sutures: | | | | |
| Gut | X | X | X | X |
| Silk | | X | X | X |
| Syrinx drain: | | | | |
| Gutta percha | X | X | | |
| Hemostatic: | | | | |
| Muscle | X | X | X | X |
| Silver clips | X | X | X | X |
| Gelfoam | | | X | X |
| Oxide cellulose | | | X | X |
| Bone wax | X | X | X | X |
| Absorbable wax | | | X | |
| Lipoidol | X | X | | |
| Thorotrast (abscess) | | | X | X |
| Metals: | | | | |
| Silver plates | X | X | | |
| Aneurysm clips (Tant.) | | | X | X |
| Tantalum plates | | | X | X |
| Powder | | | X | X |
| Cuffs | | | X | |
| Mesh | | | X | X |
| Aneurysm silver clips (locking) | | | | X |
| Steel plates | | | X | X |
| Mesh (steel) | | | X | X |
| Sutures | | X | X | X |
| Selverstone clamps | | | | X |
| Kees clips (aneurysm) | | | | X |
| Dural substitutes: | | | | |
| Cargyle membrane | X | X | X | X |
| Gelfilm | | | X | |
| Freeze-dried dura | | | | X |
| Orlon/Vinyon | | | | X |
| Bone Substitutes: | | | | |
| Autogenous graft | X | X | X | X |
| Bank bone | | | | X |
| Anorganic bone | | | | X |
| Celluloid | X | X | | |
| Tubes: (Hydrocephalus therapy) | | | | |
| Silver | X | X | X | |
| Rubber | | X | X | X |
| Plastic | | | X | X |
| Valves: (Hydrocephalus) | | | | |
| Tarlov | | | X | X |
| Pudenz | | | | X |
| Holter | | | | X |
| Radioactive seeds, etc. | X | X | X | X |
| Yttrium, etc. | | | | X |
| Implanted electrodes | | | X | X |
| and coil (induction) | | | X | X |
| Plastics: | | | | |
| Blood vessel tubes | | | X | |
| Acrylic plates | | | X | X |
| Methyl-methacrylate (Spence) | | | | X |
| Vessels (vinyon) | | | | X |
| Nerves (Millipore) | | | | X |
| Synostosis (strips) | | | X | X |
| Varnish (Aneurysm) | | | | X |
| Spray (Aneurysm) | | | | X |
| Gauze (Aneurysm) | | | | X |
| *Total* | 12 | 15 | 30 | 41 |

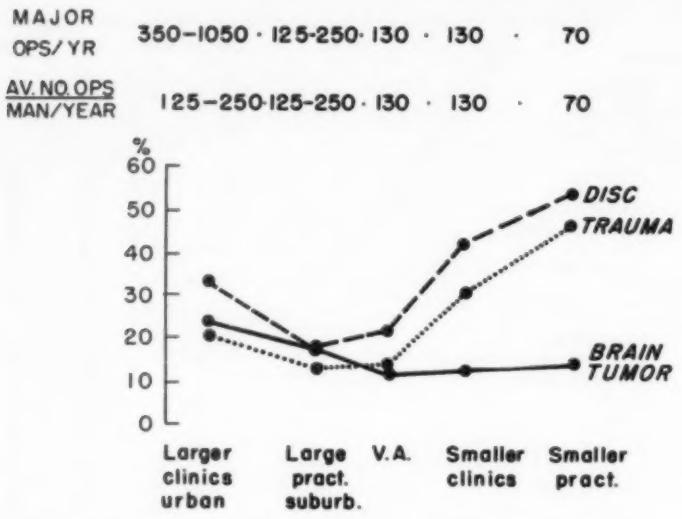


Fig. 4—Graph based on maximal percentages for each neurosurgical group.

stereotaxic surgery, perhaps of the hypothalamus, is still in its infancy, as far as potential therapeutic applications are concerned, above and beyond its use for the treatment of pain and dyskinesias.

In a word then, while the accent on neurosurgical training must always be centered on basic diagnostic, surgical and physiological principles, it seems clear that increasing attention in a training program must also be devoted to such matters as the principles and procedures of cerebral vascular surgery and the further application to neurosurgery of radioactive, ultrasonic, electronic, biochemical and stereotaxic techniques. The vistas opened up by these six rapidly developing fields alone make the future of neurological surgery look bright, provided able, imaginative, research-minded young men continue to enter this challenging branch of surgery.

At this juncture, however, it should be emphasized that research need not necessarily be restricted to a laboratory filled with expensive equipment, for there is still much to learn from sharp observation of clinical problems. Clinical research only recently has been exemplified by neurosurgical[11] and angiographic[16] observations of cerebral vaso-

spasm and by a simple, yet highly ingenious study of pain-producing structures inside the human spine[17].

Turning from the technical trends and research possibilities that can shape a neurosurgical training program, let us now look into the kind of work to which trainees may eventually look forward. This is indicated in Figure 4 by the tabulation of replies to a recent questionnaire sent to a number of colleagues practicing in small and large cities and clinics during the year 1958. Replies were gratefully received from 30 neurosurgeons* in 14 states: New York, New Jersey, Connecticut, Massachusetts, Florida and nine states west of the Alleghenies. Half of those responding were trained at the Neurological Institute of New York.

Incidentally, the small number of cases done by some men does not reflect on their skill but rather on such highly significant factors as the population saturation of their community, the diagnostic sophistication of local practitioners and neurologists, the number of years in practice, their own special interests and duties, and the fact that they themselves must do all their own lumbar punctures and of course, most other tests.

The clinical data so obtained clearly show that intervertebral disc surgery, which includes acute, degenerative and exploratory lumbar, thoracic and cervical disc operations, is the main backlog of most neurosurgeons, constituting approximately 30 per cent of their work. It is of interest that only four of the 27 neurosurgeons or clinics answering this question favored spinal fusion, while seven occasionally favored its use, and 16 never or almost never resorted to spinal fusion.

Trauma surgery, which includes both chronic and acute head, spine and peripheral nerve operations, varied in amount from one clinic or practice to another, depending on local circumstances and interests. In general, this ranged from 10 to 20 per cent in the larger metropolitan clinics of New York and other cities and in large suburban practices. In smaller suburban practices, the average approached 40 per cent of the total operative load. In such practices there was also apt to be a larger number of non-surgical trauma cases seen in consultation.

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* The author gratefully acknowledges thoughtful suggestions and data from the following neurosurgeons:
Doctors Boykin, F. C., Buermann, A., Corradini, E. W., Echlin, F. A., Fitch, T. S. P., Gang, K. M., Gross, S. W., Hoen, T. I., Kaplan, A., Mahoney, W., Negrin, J., Pierce, M. A., Ray, B. S., Stellar, S. and Tarlov, I. M.

*Trained at Neurological Institute of New York:* Doctors Brackett, C. E., Carton, C. A., Clark, K., Ehrlich, W., Galbraith, J. G., Gerol, A. Y., Krueger, E. G., Miller, L. J., Mulford, E. H., Pava, A. A., Pool, J. L., Robertson, J. W., Ryan, E. C., Siris, J. and Van Landingham, J. H.

TABLE II—NEUROLOGICAL INSTITUTE OF NEW YORK (1958)

| BENIGN TUMORS AND ELECTIVE SURGERY | *Cases* | *Deaths* | *Mortality* |
|---|---|---|---|
| *Craniotomy:* | | | |
| Benign B.T. | 75 | 2 | 2.6% |
| Elective | 60 | 0 | 0 |
| *Laminectomy:* | | | |
| Benign C.T. | 18 | 0 | 0 |
| Discs, etc. | 283 | 0 | 0 |
| | 436 | 2 | 0.4% |
| MALIGNANT TUMORS AND IMPERATIVE NEUROSURGERY | | | |
| *Craniotomy:* | | | |
| Malignant B.T. | 142 | 22 | 15.3% |
| Imperative | 146 | 6 | 4.1% |
| Aneurysms | 31 | 5 | 16.0% |
| Angiomas (AV) | 8 | 2 | 25.0% |
| *Laminectomy:* | | | |
| Malignant C.T., etc. | 60 | 2 | 3.3% |
| | 387 | 37 | 9.5% |

Brain tumor surgery comprised roughly 25 per cent of the annual number of major operations at most of the larger neurosurgical clinics, 16 per cent in larger suburban practices and 11 per cent in smaller clinics and practices. Postoperative results, it must be frankly stated, were not always as good for benign tumor surgery in some of the smaller practices as in the larger clinics, where staff experience and day and night coverage by specially trained personnel lead to an appreciable reduction in mortality and complications. Table II, for example, shows that the mortality rate for benign brain tumors and elective neurosurgery at the Neurological Institute of New York during the past year, 1958, was close to zero (0.4 per cent). For malignant or metastatic tumors, acute injuries of the brain and spinal cord, and ruptured intracranial aneurysms, the total rate was of course higher, being 9.5 per cent.

With respect to intracranial aneurysm surgery, replies from the 27 neurosurgeons who answered this question listed a total of 191 aneurysms surgically treated during the year 1958. Five men did no aneurysm surgery at all, and nine no intracranial aneurysm surgery, while a few operated on as many as 10 to 20 aneurysms during the year. One

hundred twenty-seven aneurysms were directly occluded by intracranial surgery, while 64 were treated by carotid ligation in the neck, the ratio of intracranial to carotid ligation surgery being 3 or 4 to 1 in most of the larger clinics, 2 to 1 in most of the larger suburban practices and 1 to 1 or less in most smaller clinics and practices.

The percentages of various types of tumors and other conditions treated by neurosurgeons were remarkably constant from one clinic or practice to the next, and coincided closely with published figures. Aside from disc, trauma and tumor surgery, each clinic listed only one or two procedures, such as operations for pain, dyskinesia, hypophysectomy or hydrocephalus, that constituted over 5 per cent but less than 20 per cent of their total operative load. In most instances, each of such special procedures therefore comprised no more than 5 per cent and usually less than 5 per cent of the total work.

Altogether, examination of the work load in various clinics and practices suggests that the neurosurgeon headed for a non-academic independent career will be particularly concerned with the management of disc and trauma problems, which together may comprise more than two-thirds of his practice (Figure 4).

The neurosurgeon headed for large clinics and practices, therefore, should not only be especially well trained in brain tumor and aneurysm work, but also in other highly specialized types of neurological surgery, such as pallidal, pain-relieving, pituitary and other procedures which are often so dependent on special equipment, close teamwork with other specialists, and continuous rather than sporadic experience. The philosophy of this thought is illustrated by the management of intracranial aneurysms.

At some of the larger neurosurgical clinics, for example, it has been found that concentration on a problem such as aneurysm therapy by a team of a few neurosurgeons, neurologists, neuroradiologists and anesthesiologists leads to far better results[18] than the results of the occasional or "casual" aneurysm surgeon. Good results are abetted by concerted experience in the selection of cases for a given procedure, experience in the use of hypothermia and other ancillary aids, and so on. In this way the mortality rate for intracranial aneurysm surgery has been reduced from a previous figure of 26 per cent to as low as 11 per cent.

Improvements in the surgery of acoustic nerve tumors[19, 20] have likewise been the result of concerted effort, which has lowered the mor-

tality rate and complications from over 20 per cent ten years ago to less than 10 per cent for the past 5 years and zero for the past year, as indicated by our own records, which show that 13 such tumors were operated upon during the past year without a loss. These results are mentioned because they indicate that the more difficult and hazardous neurosurgical problems can, as a rule, be handled so satisfactorily in specially staffed and equipped hospitals.

This may well mean that future neurosurgeons will tend to have less tumor and aneurysm work unless they are affiliated with clinics or centers staffed and equipped for the proper management of such problems. To remedy this situation, it might be wise to encourage at least one hospital in each large suburban community to become a neurosurgical center, as suggested by several colleagues in the recent questionnaire. Such a system might not only prevent more complications, but could also reduce the endless and grossly inefficient travelling of many neurosurgeons from one hospital to five or six others each day. This problem might also be solved by granting courtesy privileges at special centers where neurosurgeons could operate on their more unusual or difficult cases. We are now exploring this possibility at the Neurological Institute for one or two of our own recent graduates.

What do our colleagues now suggest as to neurosurgical training needs? The majority of those who have expressed themselves on this subject urge two years' general surgical experience and at least one year of neurological training. In general surgery, as some have pointed out, attention should be especially directed to knowledge of electrolyte and fluid balance, vascular, plastic, and head and neck surgery, as well as to other branches whose techniques are so often of crucial value in neurological surgery.

Ample training in neurology is stressed by all, and particularly by those practicing in suburban communities, where neurosurgeons must of necessity be their own neurologists owing to the existing dearth of neurologists.

Trauma surgery and management was also stressed as an urgent training need, and it was repeatedly suggested that centers lacking an adequate number of trauma cases should arrange an exchange system so that residents could gain this type of experience elsewhere. This matter is now being looked into by some of us.

With respect to trauma training, many colleagues have urged formal

instruction in the medico-legal aspects of practice. As one man put it, "like the young bride, I wish someone had told me". I must agree with the soundness of this idea, particularly as it has become evident that most neurosurgeons deal with a large volume of compensation cases and, incidentally, consider it a privilege to be of service in this important and often neglected field.

Everyone agreed that training programs should emphasize the basic sciences such as neuroanatomy and neuropathology, and that men headed for an academic career should put in at least a year in the research laboratory on neurophysiological or similar work. Over and over again it was also pointed out that familiarity with electroencephalography and especially with x-ray diagnosis is imperative, as young neurosurgeons generally have to interpret by themselves their own myelogram, arteriogram and encephalogram films. Even though a formal course in x-ray diagnosis is offered, the only way to acquire proficiency in x-ray diagnosis, in my opinion, is for each man, throughout his training, *always* to make his own x-ray diagnosis with a statement of his reasons.

While it may safely be predicted that the future of neurosurgery looks bright, it is also true that much investigative work needs to be done, not only for the sake of basic research but also for the practical development of new fields and techniques in trauma, tremor, tumor, pain and other types of neurosurgery that will serve to expand its scope and activity. To do this, however, it will be necessary to set up more postgraduate fellowships with salaries that will match or approximate the income a resident could otherwise expect after completing his training. Already many capable men have been lost to a career of disc surgery when they might have continued in a research capacity. This challenge is being met at the Neurological Institute by the appointment for the coming two years of two gifted graduating residents as research fellows.

What of teaching? Practice in this sphere is generally ample in that residents participate in lectures to nursing and student groups. Following graduation, even those neurosurgeons not affiliated with a university hospital engage in a good deal of teaching in the form of talks and lectures to local hospital medical staffs and societies. This of course is most important, especially in communities eager for neurological and neurosurgical orientation. For without proper diagnostic sophistication, a cord tumor may too long be considered a case of multiple sclerosis;

focal epilepsy due to a brain tumor may too long be treated as idiopathic epilepsy, while a supposed stroke may never be properly diagnosed if actually due to an aneurysm, angioma, carotid thrombosis or intracortical hemorrhage.

As to research responsibility, one gains the impression that even though trainees are encouraged to work in the laboratory and write one or more clinical papers, once in practice they are apt to neglect investigative work and may not even write up interesting and important cases. The latter, however, is a form of research, clinical to be sure, that every neurosurgeon, no matter how busy, owes to his specialty as well as to the medical profession.

In summary, this stock-taking of neurosurgery points to a bright future, not only because of the many new fields to conquer but also because of the need for further work on existing problems.

Neurosurgical training, as we have seen, should clearly include experience in the basic sciences and allied fields, among which neurology is so especially important. Each trainee, moreover, must be certain that he makes himself adept in x-ray interpretation as he goes along, for he will so often have to rely entirely on his own diagnostic acumen for the duration of his career.

Training should include instruction in traumatic and medico-legal problems, and practice in making contributions to the literature, for these are responsibilities of every neurosurgeon. Those planning on an academic career should be exposed to as long and comprehensive a training program as possible, and should have the opportunity of exchange visits to other centers. When all is said and done, each man must obviously train himself not only with a view to more effective patient care but with the added aim of improving neurosurgical procedures and management as he goes along. As Dr. Frank Turnbull[21] put it, "Neurosurgery is what you make it".

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# NEW YORK HEART ASSOCIATION

## ABSTRACTS OF PAPERS

Presented at the Scientific Session held at The New York Academy of Medicine, April 21, 1959

## *Reactivity of the Systemic and Renal Arterioles to L-Norepinephrine In Essential Hypertension (Abstract)*

ERVIN A. GOMBOS AND WILLIAM GOLDRING

Department of Medicine, New York University College of Medicine, New York

Evidence has been collected by others suggesting that constriction of the systemic arterioles is more susceptible to norepinephrine in hypertensive patients than in normotensive subjects.

We undertook to reexamine this problem and studied the effect of infusion of L-norepinephrine in graduated doses in 4 normotensive subjects and 17 hypertensive patients. Observations were made on systemic arterial pressure and on glomerular filtration rate and renal plasma flow. Infusion of L-norepinephrine increased mean arterial pressure in a comparable manner in normotensive and hypertensive individuals. Effect on glomerular filtration rate showed no significant difference between the two groups studied. Norepinephrine decreased renal plasma flow in normotensives more than in hypertensives in absolute values as well as percentage change. In view of the greater decrease in renal plasma flow in normotensives, as would be expected, norepinephrine induced a greater increase in renal resistance in normotensive subjects than in hypertensive patients. This fact was further corroborated by the relatively greater increase in filtration fraction in normotensive subjects. A further indication of the relatively greater reactivity of the renal arterioles in normotensive subjects compared to hypertensive patients is the fact that during the maximal dose of norepinephrine the per cent increase in renal resistance was greater in the normotensive subjects.

These observations were repeated in normotensive and hypertensive individuals after prolonged salt deprivation. The extent of norepinephrine-induced systemic vasoconstriction was unaltered by salt restriction in both groups, and renal plasma flow was decreased and renal resistance increased to the same extent in both normotensive subjects and hypertensive patients.

Our data do not support the view that the vasoconstrictive effect of infused L-norepinephrine on either systemic or renal arterioles is greater in hypertensive patients than in normotensive subjects.

## *Cardiotonic Nucleosides* (Abstract)*

N. M. Buckley, K. K. Tsuboi, Ph.D., and N. J. Zeig, B.S.

Department of Physiology, Albert Einstein College of Medicine; Department of Pediatrics, Cornell University Medical College, New York, N. Y.

The effects of certain naturally occurring nucleosides on acute left ventricular failure was studied in 15 isolated dog hearts. Using a preparation in which only the left ventricle performed external work, unilateral failure was produced by exposure of the ventricle to elevated aortic pressure. Parameters of left ventricular function used to evaluate the control, failure and nucleoside periods included stroke work and contractility. Administration of the nucleosides (available to the myocardium in concentrations of $4 \times 10^{-5}$ molar) was accompanied by reproducible effects on the ventricle after failure.

Adenosine and cytidine were found to further decrease stroke work and contractility. Guanosine, inosine, thymidine and uridine were found to restore or exceed the control level of work and contractility. On the basis of separate metabolic studies with dog blood, it was concluded that only limited degradation of the nucleosides by blood enzymes could have occurred. The effects on the ventricle were shown to be independent of heart rate, chamber size and coronary supply. The compounds apparently could be classified as positive or negative inotropes according to the substituent groups on the 6-carbon of the pyrimidine ring. Further work on this relationship of structure and function is in progress.

* Presented at the Scientific Session of the New York Heart Association held at The New York Academy of Medicine, April 21, 1959.

Supported by grants from the American Heart Association, the Life Insurance Medical Research Fund and the Commonwealth Fund.

## *An Experimental Procedure for Correction of Transposition of the Great Vessels* (Abstract)*

Philip Glotzer, Allan E. Bloomberg and Elliott S. Hurwitt

The Henry L. and Lucy Moses Surgical Research Laboratories, the Montefiore Hospital, New York, N. Y.

There is no standard procedure for the correction of transposition of the great vessels. The need for such a procedure is clear from the fact that this defect is the largest cause of infant mortality from congenital heart disease. Venous transposition should offer the most likely possibility of successful correction of this condition because of the great technical difficulty in transposing the associated coronary arteries. A procedure producing total intracardiac venous transposition has been devised, and demonstrated in dogs to accomplish this end. The operation is done under conditions of cardiopulmonary bypass with potassium

* Presented at the Scientific Session of the New York Heart Association held at The New York Academy of Medicine, April 21, 1959.

Aided by a grant from the New York Heart Association.

citrate arrest. The entire intra-atrial septum is excised converting the two atria into one large chamber. An artificial septum of crimped and knitted dacron is placed so as to exclude the entire pulmonary venous drainage and the tricuspid orifice from the remaining common chamber. This results in flow of the systemic venous blood into the left ventricle through the atrial defect and mitral valve; the entire pulmonary venous drainage is shunted directly into the right ventricle through the tricuspid orifice. Mixing is prevented by the artificial septum. The intracardiac manipulations have averaged 35 minutes of cardiopulmonary bypass. Studies by angiogram and oxygen saturation have demonstrated the venous transposition.

The procedure as described has been applied to a clinical case unsuccessfully, death having resulted from a technical error in the use of the pump oxygenator, resulting in fatal over-transfusion. The procedure itself, however, proved to be perfectly feasible, and seemed to be technically satisfactory at autopsy.

## *The Effect of Synthetic Vasopressins on Adrenal Cortical Secretion** *(Abstract)*

LOUIS F. SCIAN†, GEORGE DERMKSIAN, WILLIAM F. HAYNES, JR., AND JAMES G. HILTON

Department of Medicine, St. Luke's Hospital, New York, N. Y.

Adrenocortical steroid output, as influenced by synthetic vasopressins, was determined by the method of Hilton and associates (*Amer. J. Physiol. 192*:525, 1958), employing an aortic pouch perfusion.

Both synthetic arginine and synthetic lysine vasopressin were shown to have a stimulatory effect on the adrenal cortex comparable to that achieved with ACTH in the hypophysectomized dog adrenal preparation perfused with hypophysectomized donor blood. In 15 experiments hydrocortisone secretion from the perfused adrenal glands during control periods averaged less than 1γ per minute. Following stimulation with vasopressin (0.1 - 0.4 units per minute for 7 minutes) a six-fold rise in secretion rate was noted. This was associated with a blood pressure rise within the pouch averaging 25 mm.Hg. A similar pressor response evoked by norepinephrine had no effect on steroid secretion. In several experiments the stimulation achieved by vasopressin equalled or exceeded that of a maximal ACTH dose (1 unit per minute for 7 minutes).

It is concluded that vasopressin has a marked adrenocortical stimulatory effect and may play an important role in the stress reaction.

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Supported in part by a grant from the New York Heart Association.

† Fellow of the New York Heart Association.

# *Intermittent Positive Pressure Breathing in Patients with Pulmonary Heart Disease: Its Effect on Distribution of Inspired Air* (Abstract)*

GLORIA E. TORRES AND HAROLD A. LYONS

Department of Medicine, State University of New York, Downstate Medical Center, Brooklyn, N. Y.

One of the primary considerations in the treatment of pulmonary heart disease is directed at the improvement of the ventilation of the lung. Intermittent positive pressure breathing is a modern and frequent measure used for this purpose. Although reports have been made of its effectiveness or noneffectiveness, no reports have been made of its mode of action nor have studies of ventilation been made during its actual administration.

The measurement of the effect of intermittent positive pressure breathing on the distribution of the inspired air, and the number and types of ventilatory spaces in patients with pulmonary emphysema and pulmonary heart disease were made before and during the actual administration of intermittent positive pressure breathing.

Twelve patients and ten control subjects were studied both before and during intermittent positive pressure breathing. The functional residual capacity, continuous nitrogen washout curves with 100 per cent oxygen breathing by means of a nitrogen analyzer were made. The size and number of the ventilatory spaces were calculated and plotted and the Fowler index was measured.

The data obtained showed that in the patients with pulmonary heart disease there was over 100 per cent increase in functional residual capacity, four to six spaces of ventilation, with the poorly ventilated spaces comprising usually above 50 per cent of the whole. During intermittent positive pressure there was a decrease in size and number of ventilated spaces to as few as three in some cases, with the P.V.S. being significantly reduced and the Fowler index being markedly reduced and approaching the normal. Concomitant elevation of arterial oxygen tensions and decrease in arterial carbon dioxide tension occurred.

It may be concluded from this study that intermittent positive pressure breathing given to the patient with pulmonary heart disease improves the distribution of inspired air, decreases or abolishes the poorly ventilated spaces and thus improves alveolar ventilation.

* Presented at the Scientific Session of the New York Heart Association held at The New York Academy of Medicine, April 21, 1959.

# *The Mimetic Nature of Rheumatic Fever Recurrences* (Abstract)*

ALVAN R. FEINSTEIN AND MARIO SPAGNUOLO

Irvington House, Irvington-on-Hudson, N. Y. and the Department of Medicine, New York University College of Medicine, New York, N. Y.

Valvular involvement—manifested by diastolic and/or apical unequivocally-organic systolic murmurs—has been shown to have important prognostic significance in acute rheumatic fever. Patients without valvulitis remained free of heart disease. Recurrences of rheumatic fever are considered dangerous because they may increase cardiac damage or may bring it to patients who did not acquire it with the first attack.

The latter concept has now been re-examined. The present work demonstrates that recurrent attacks of rheumatic fever frequently have mimetic and repetitive patterns in the same individual, consistent with the following hypotheses:

1. Patients who do not have valvular involvement in the first attack do not get it with subsequent attacks.
2. Patients who eventually have rheumatic heart disease show evidence of valvulitis in their *first* attack. In these individuals, recurrences are particularly to be feared because the cardiac damage may recrudesce or increase.

The data to support these hypotheses come from an analysis of the rheumatic episodes in 161 patients who had two or more attacks. Each of the 370 attacks fulfilled the modified Jones' diagnostic criteria. Each patient had been treated at Irvington House during the most recent attack and had been followed monthly thereafter on anti-streptococcal prophylaxis. Although arthritis, chorea and/or erythema marginatum showed individual recurrent patterns, these noncardiac features will not be further discussed here.

The analysis of valvular involvement showed the following: 61 patients conformed to hypothesis 1) above. Despite multiple rheumatic attacks, they remained free of heart disease. Ninety patients conformed to hypothesis 2). In each instance, evidence of valvular involvement appeared with the *first* attack. Recurrent attacks in this group brought a recrudescence of valvulitis, worsening of the cardiac status, or evidence of new valvular damage. Ten patients failed to conform to hypothesis 1) or 2), and showed a diastolic murmur during a later attack although none was recorded at the first attack. In eight of these patients, however, the data clearly indicated the likelihood that the diastolic murmur was present at the first attack but had not been recognized. The remaining two patients were the only significant exceptions to the stated hypotheses.

These results suggest that patients have an inherent and persistent susceptibility which predetermines the tissues involved in rheumatic inflammation. There are also evident clinical implications for the selection of rheumatic patients for continuous and indefinite antistreptococcal prophylaxis.

* Presented at the Scientific Session of the New York Heart Association held at The New York Academy of Medicine, April 21, 1959.

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*Brown, S. S.; Libo, H. W., and Nussbaum, A. H.: Norethandrolone in the Successful Management of Anorexia and "Weight Lag" in Children, Scientific Exhibit presented at the Annual Meeting of the American Academy of Pediatrics, Chicago, Oct. 20-23, 1958.

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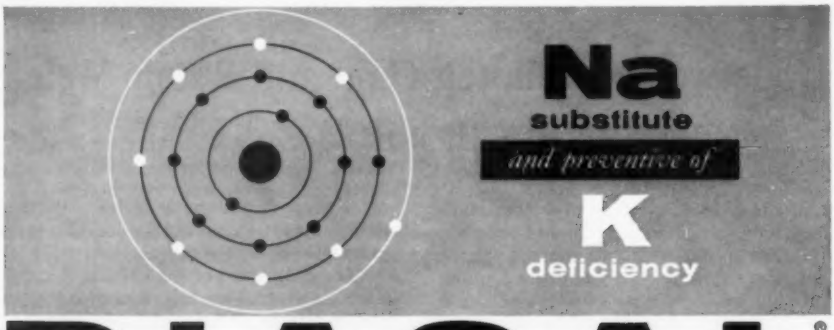


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Ensey, J. E.: Am. J. Obst. 77:155, 1959

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*Green, J. R., & Steelman, H. F: Epileptic Seizures, Baltimore, Williams & Wilkins Company, 1956, p. 136.

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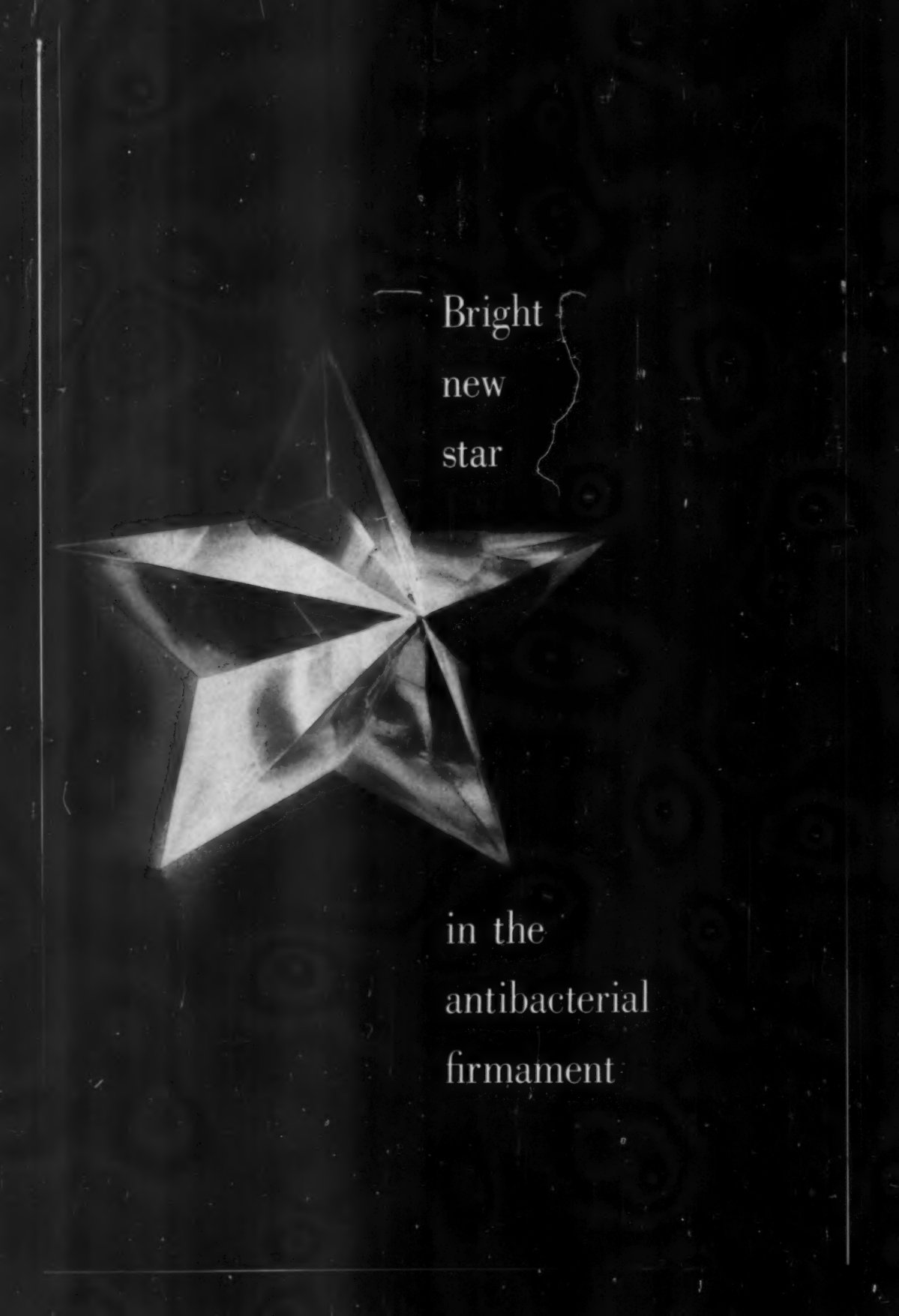
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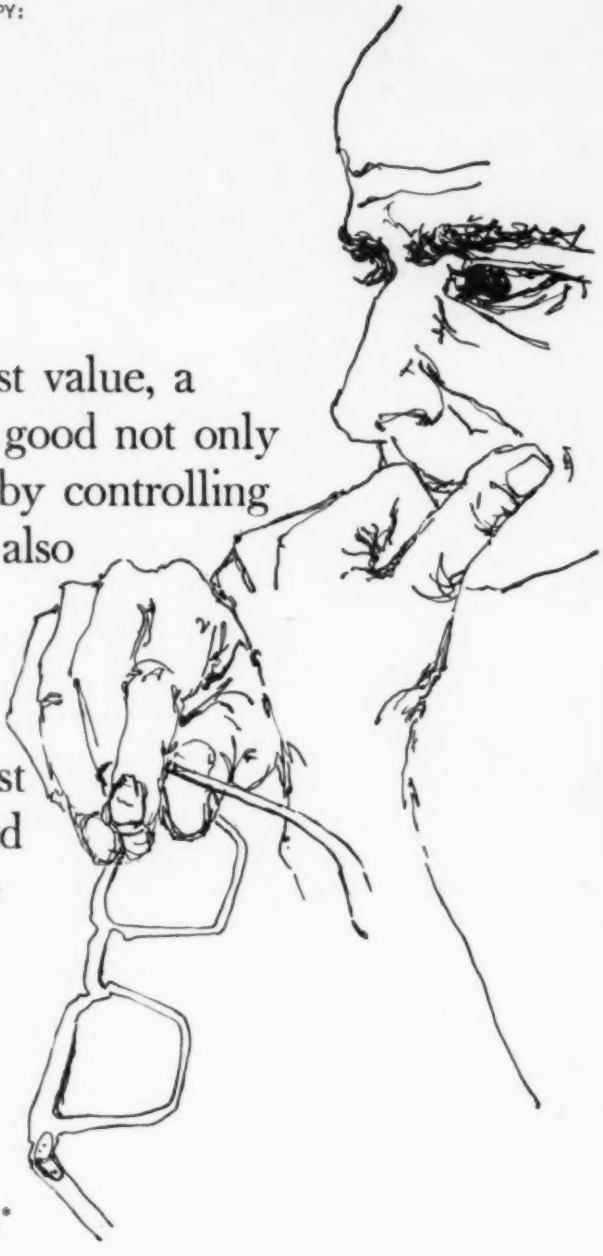

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